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SPECIAL ISSUE

Noninvasive Positive Pressure Ventilation

- Consensus Statement: NPPV
- History & Terminology
- Characteristics of Pressure-Targeted Ventilators
- Face vs Interface
- Applications of NPPV in Respiratory Failure
- Prevention of Ventilatory Failure due to Inadequate Pump Function
- Pediatric Application of Noninvasive Ventilation
- Success & Failure of NPPV in Adult Acute Care Applications
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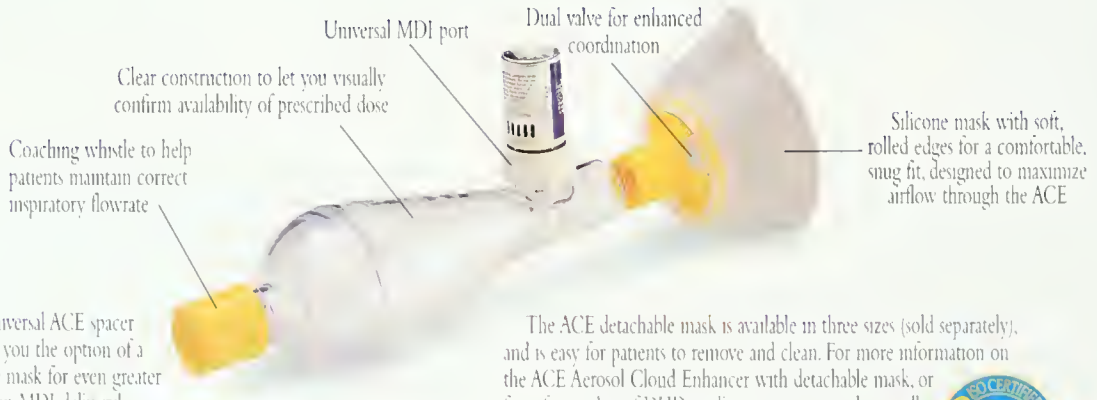
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Contents ...

April 1997
Volume 42, Number 4

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CONSENSUS CONFERENCE IV
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THE PROCEEDINGS OF A CONFERENCE HELD
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CONFERENCE PROCEEDINGS

362 Consensus Conference IV: Preamble and Consensus Statement

370 Noninvasive Positive Pressure Ventilation: History and Terminology
by David J Pierson—Seattle, Washington

380 Characteristics of Pressure-Targeted Ventilators Used for Noninvasive Positive Pressure Ventilation
by Robert M Kacmarek—Boston, Massachusetts

389 NPPV: Face versus Interface
by Robert E Turner—Marietta, Georgia

394 Continuous and Periodic Applications of Noninvasive Ventilation in Respiratory Failure
by Richard G Wunderink—Memphis, Tennessee, and Nicholas S Hill—Providence, Rhode Island

403 The Prevention of Ventilatory Failure due to Inadequate Pump Function
by John R Bach—Newark, New Jersey

414 Pediatric Application of Noninvasive Ventilation
by W Gerald Teague—Atlanta, Georgia

424 Noninvasive Positive Pressure Ventilation: Predictors of Success and Failure for Adult Acute Care Applications
by Dean Hess—Boston, Massachusetts

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... Contents

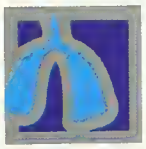
April 1997
Volume 42, Number 4

432 Complications of Noninvasive Mask Ventilation
by Nicholas S Hill—Providence, Rhode Island

443 Study Design in the Evaluation of Noninvasive Positive Pressure Ventilation
by Gordon D Rubenfeld—Seattle, Washington

IN THIS ISSUE

347 AARC Membership Application
342 Abstracts from Other Journals
464 Advertisers Index & Help Lines
464 Author Index
457 Calendar of Events
453 Call for Open Forum Abstracts
460 Manuscript Preparation Guide
455 MedWatch
458 New Products & Services
450 Notices



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Editorials, Commentaries, and Reviews To Note

"Inactive" Ingredients in Pharmaceutical Products: Update (Subject Review)—CM Berlin Jr, DG McCarver, DA Notterman, RM Ward, DN Weismann, GS Wilson, JT Wilson, the American Academy of Pediatrics Committee on Drugs. Pediatrics 1997;99(2):268-278.

Lung and Heart-Lung Transplantation in Children (State of the Art)—BE Noyes, G Kurland, DM Orenstein. Pediatr Pulmonol 1997;23:39-48.

Immunosuppressive and Cytotoxic Pharmacotherapy for Pulmonary Disorders (State of the Art)—JP Lynch III, WJ McCune. Am J Respir Crit Care Med 1997;155:395-420.

β_2-Agonist Metered Dose Inhaler Overuse: Psychological and Demographic Profiles—JL Beausoleil, DP Weldon, SJ McGeady. Pediatrics 1997;99(1):40.

OBJECTIVE: To identify psychological and demographic correlates of children and adolescents known to overuse β_2-agonist metered dose inhalers (β-MDIs). DESIGN: During residential care for severe asthma, demographic and psychological characteristics of 17 children and adolescents known to be β-MDI overusers were compared with 38 asthmatic subjects of similar age without such history. RESULTS: β-MDI overuse occurred among all groups; however, males, minorities, and those from lower socioeconomic groups were over-represented. Overusers scored significantly lower on standardized IQ tests. Subtests of arithmetic for numeric reasoning, comprehension for understanding of social values, and picture completion for visual attention to detail were also significantly lower in β-MDI overusers, as were reading achievement tests. Testing also revealed tendencies toward dominant, shrewd, and undisciplined personality traits in the overusers. CONCLUSION: Recognition of these characteristics of children prone to β-MDI overuse will raise the clinician's awareness of this potential. Greater efforts and alternative approaches toward education and treatment of the at-risk patient and family are indicated.

Population and Occupational Screening for Obstructive Sleep Apnea: Are We There Yet?—MJ Baumel, G Maislin, AI Pack. Am J Respir Crit Care Med 1997;155:9.

Several features of obstructive sleep apnea (OSA) suggest that it may be an appropriate disease for screening programs for general populations and more specific high-risk groups. Preliminary data suggest that OSA represents an important health problem in terms of high prevalence, increased levels of morbidity and mortality, and increased public safety risk. Furthermore, the chronicity of the disease and the relatively low levels of recognition of the disorder in the medical community suggest a potential for lead-time gains for screening programs. Specific groups that might be considered for screening programs include commercial vehicle operators, hazardous duty personnel, and certain groups of medical patients. The purpose of this clinical commentary is to consider the issues of population and specific group screening for OSA by reviewing the general principles of screening for chronic disease and then applying these principles specifically in the case of OSA. More extensive outcomes data relating levels of severity of the disorder to its potential adverse outcomes are needed and will assist in tailoring appropriate screening programs and determining the cost-effectiveness of screening various populations.

An Inhaled Glucocorticoid Does Not Prevent Tolerance to the Bronchoprotective Effect of a Long-Acting Inhaled β_2-Agonist—DH Yates, SA Kharitonov, PJ Barnes. Am J Respir Crit Care Med 1996;154:1603.

There is increasing evidence for the development of tolerance to the protective effects of inhaled β_2-agonists against bronchoconstrictor stimuli. Animal studies have suggested that glucocorticoids protect against the down-regulation of β_2-receptors after chronic exposure to β_2-agonists. In a double-blind placebo-controlled crossover study in 12 patients with mild asthma, we investigated the effect of inhaled budesonide or identical placebo on the protection conferred by albuterol (200 μg) against methacholine-induced bronchoconstriction before and after treatment with the long-acting β_2-agonist salmeterol. Patients were randomized to be treated for 3 weeks with inhaled budesonide (800 μg twice a day) or placebo; salmeterol (50 μg twice a day) was added during the third week. Airway responsiveness to methacholine was measured 15 minutes after abuterol, both before and exactly 23 hours after the last salmeterol dose. Mean FEV_1 increased significantly after 2 weeks of budesonide ($p < 0.05$) and increased further after salmeterol ($p < 0.05$) compared with placebo. After 2 weeks, the bronchoprotective effect of albuterol against methacholine was significantly greater with budesonide than with placebo (3.4 vs 2.4 doubling dilutions; $p < 0.05$), consistent with an improvement in airway hyper-responsiveness with budesonide therapy. However, regular salmeterol treatment for 1 week significantly diminished the protection conferred by albuterol against methacholine challenge, both with budesonide and with placebo (-1.1 ± 0.42 and -1.41 ± 0.30 doubling dilutions, respectively). There was no significant difference in the loss of bronchoprotection seen with salmeterol between budesonide and placebo treatment periods. Our study suggests that even a high dose of an inhaled glucocorticoid fails to prevent the loss of bronchoprotection produced by regular β_2-agonist therapy.

Bronchodilators and Acute Cardiac Death—S Suissa, B Hemmelgarn, L Blais, P Ernst. Am J Respir Crit Care Med 1996;154:1598.

Bronchodilators used in the treatment of airway disease have been shown to have a variety of cardiac effects that may contribute to the occurrence of life-threatening events such as cardiac arrhythmias and cardiac arrest. We investigated whether theophylline and β-agonists were associated with cardiovascular mortality among a cohort of subjects prescribed antiasthma medications. We used a population-based cohort of 12,301 subjects aged 5 to 54 years, formed from health-insurance databases from Saskatchewan, Canada, and spanning the period 1978 to 1987. Within this cohort, we

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REFERENCES 1. Data on file, HealthScan Products Inc. Results of aerosol testing with albuterol, beclomethasone, and cromolyn sodium. 2. Data on file, HealthScan Products Inc. Results of gamma-scintigraphy aerosol deposition studies. 3. Gibson PG, Wlodarczyk JH, Borgas T: Drug delivery in asthma: A comparison of spacers with a jet nebuliser. *Aust NZ J Med* 25:324-329, 1995.

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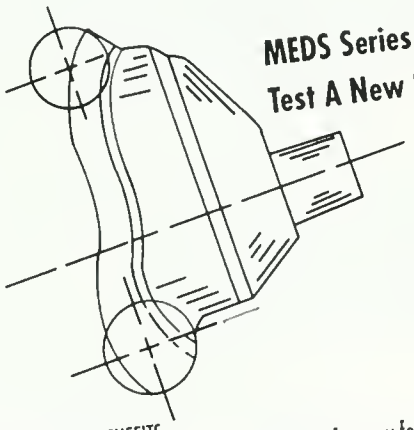
identified all 30 deaths from cardiovascular causes in which acute asthma did not appear to be a contributing factor. We identified all asthma and cardiovascular drugs dispensed to these subjects shortly before their deaths and compared this therapy to that dispensed to a random sample of 4,080 person-time controls. After adjustment for age and the prior use of cardiac drugs, the rate of cardiovascular death was greater in users of theophylline, with a rate ratio (RR) of 2.7 (95% CI: 1.2 to 6.1), and in users of β-agonists taken orally or by nebulizer (RR = 2.4; 95% CI: 1.0 to 5.4), but not in users of β-agonists administered by metered dose inhaler (RR = 1.2; 95% CI: 0.5 to 2.7). The great majority of cardiovascular deaths occurred among subjects with clinical or pathologic evidence of potentially lethal conditions. These results suggest that the use of theophylline and of β-agonists administered orally or by nebulization should be avoided in subjects with significant cardiac disease or at high risk for such disease, especially acute coronary insufficiency and congestive cardiomyopathy. On the other hand, the use of β-agonists administered by metered dose inhalers (MDIs) was not associated with an increased risk of cardiovascular death. *See the related editorial:* ***Identifying Patients at Risk from the Use of Beta-adrenergic Agonists—AR Leff. Am J Respir Crit Care Med 1996;154:1593.***

Attitudes Regarding Advance Directives Among Patients in Pulmonary Rehabilitation—JE Heffner, B Fahy, L Hilling, C Barbieri. Am J Respir Crit Care Med 1996;154:1735.

We performed a cross-sectional, descriptive questionnaire study in 2 pulmonary rehabilitation programs to assess: (1) attitudes of 105 subjects with chronic lung conditions about end-of-life decision-making; (2) the determinants of these attitudes; and (3) patient acceptance of rehabilitation programs as foci for education about advance directives (ADs). We found that 99 of the 105 subjects (94.3%) had health worries, the most common of which was fear of increasing dyspnea (33.3%). Although 93.8% had opinions about intubation, less than 42% had completed an AD. Most subjects wanted information about ADs (88.6%) and life-support (68.6%); pulmonary rehabilitation programs, lawyers, and physicians were preferred sources for AD information. Although 98.9% of the patients wanted patient-physician AD discussions, only 19.0% had such discussions, only 15.2% had discussed life-support, and only 14.3% thought that their physicians understood their end-of-life wishes. Subject willingness to undergo intubation varied with baseline health, likelihood of survival, and anticipated health following extubation. We conclude that patients in pulmonary rehabilitation programs desire more information about end-of-life issues than is currently provided by physicians. They regard pulmonary rehabilitation educators as valuable sources of AD education.

Influence of Gender and Endotracheal Tube Size on Pre-Extubation Breathing Pattern—SK Epstein, RL Ciubotaru. Am J Respir Crit Care Med 1996;154:1647.

An imbalance between work of breathing and respiratory muscle capacity often results in rapid, shallow breathing (increased respiratory rate/tidal volume [f/V_T]). Because this imbalance commonly causes unsuccessful weaning from mechanical ventilation, it is not surprising that an elevated f/V_T accurately predicts weaning failure. However, while studying extubation outcome, we



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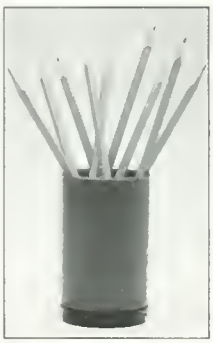

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observed that women and patients with narrow endotracheal tubes are often successfully extubated with an elevated f/V_T. We studied 218 medical patients in the intensive care unit who had a f/V_T measured through an oral endotracheal tube (off of ventilatory support) during 1 minute of spontaneous respiration at the onset of a weaning trial that culminated in extubation. Men and women were comparable at the onset of mechanical ventilation and weaning trials in severity of illness, etiology of respiratory failure, ventilator settings, and gas exchange data. Women were found to have a higher f/V_T (79 ± 5 vs 56 ± 3 breaths/L, $p < 0.001$), lower tidal volumes (381 ± 14 vs 494 ± 13 mL, $p < 0.001$), and higher respiratory rate (26 ± 1 vs 24 ± 1, $p < 0.05$). The differences persisted after controlling for extubation outcome. Smaller endotracheal tubes were associated with a higher f/V_T, especially for women (≤ 7 mm, 86 ± 6 vs > 7 mm, 68 ± 6, $p < 0.05$). Women were more likely to have a $f/V_T \geq 100$ (19/82 [women] vs 10/136 [men], $p < 0.001$). Although the overall incidence of extubation failure was similar (11/82 [women] vs 23/136 [men], p = NS), among patients with $f/V_T \geq 100$, men were more likely to require reintubation (3/19 [women] vs 5/10 [men], $p = 0.08$). We conclude that women, especially when breathing through small endotracheal tubes, have a higher f/V_T (including likelihood of $f/V_T \geq 100$) than men, independent of extubation outcome. Consideration of factors that elevate the f/V_T, unrelated to physiologic work of breathing and respiratory muscle capacity, should improve application of this index to extubation decision making.

Serum Albuterol Levels in Mechanically Ventilated Patients and Healthy Subjects after Metered Dose Inhaler Administration—AG Duarte, R Dhand, R Reid, JB Fink, PJ Fahey, MJ Tobin, JW Jenne. Am J Respir Crit Care Med 1996;154:1658.

In mechanically ventilated patients, systemic blood levels of inhaled drugs reflect absorption from the lower respiratory tract alone since, unlike non-intubated patients, oropharyngeal and gastrointestinal absorption cannot occur. To determine the efficiency of aerosol administration by a metered dose inhaler (MDI), we measured serum albuterol levels after administration by a MDI and spacer to 9 mechanically ventilated patients (10 puffs) and to 10 healthy subjects (6 puffs). Serum albuterol levels (± SEM) quantitated by high-performance liquid chromatography and electrochemical detection were: 0.09 ± 0.04 mg/mL/puff at baseline, 0.66 ± 0.10 at 5 minutes, 0.98 ± 0.10 at 10 minutes, 0.56 ± 0.08 at 15 minutes, and 0.37 ± 0.03 at 30 minutes in mechanically ventilated patients versus zero at baseline, 0.89 ± 0.12 at 5 minutes, 1.27 ± 0.13 at 10 minutes, 0.84 ± 0.09 at 15 minutes, and 0.53 ± 0.07 at 30 minutes in control subjects ($p \geq 0.07$ at 5, 10, and 30 min; $p \leq 0.05$ at baseline and at 15 min). Area under the curve ($AUC_{0\text{-}30}$) in the mechanically ventilated patients was 16.8 ± 1.4 versus 23.4 ± 1.9 ng/mL/puff × min in control subjects ($p = 0.014$). In summary, administration of albuterol with a MDI achieved a profile of serum levels in mechanically ventilated patients similar to that in healthy control subjects, but the peak serum level and systemic bioavailability ($AUC_{0\text{-}30}$) were lower in the patients. In conclusion, serum levels reliably assess lower respiratory tract deposition of albuterol, and show that MDIs are more efficient for aerosol delivery in mechanically ventilated patients than was previously reported in studies using radiolabeled aerosols.

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American Association for Respiratory Care
Membership Application

Please read the eligibility requirements for each of the classifications in the right-hand column, then complete the applicable section. All information requested below must be provided, except where indicated as optional. See other side for more information and fee schedule. Please sign and date application on reverse side and type or print clearly. Processing of application takes approximately 15 days.

- ☐ Active
- Associate
  - ☐ Foreign
  - ☐ Physician
  - ☐ Industrial
- ☐ Special
- ☐ Student

Last Name _____

First Name _____

Social Security No. _____

Home Address _____

City _____

State _____ Zip __ __ __ __ __ - __ __ __ __

Phone No. (_____) _____

Primary Job Responsibility (check one only)

- ☐ Technical Director
- ☐ Assistant Technical Director
- ☐ Pulmonary Function Specialist
- ☐ Instructor/Educator
- ☐ Supervisor
- ☐ Staff Therapist
- ☐ Staff Technician
- ☐ Rehabilitation/Home Care
- ☐ Medical Director
- ☐ Sales
- ☐ Student
- ☐ Other, specify _____

Type of Business

- ☐ Hospital
- ☐ Skilled Nursing Facility
- ☐ DME/HME
- ☐ Home Health Agency
- ☐ Educational Institution
- ☐ Manufacturer or supplier
- ☐ Other, specify _____

Date of Birth (optional) _____ Sex (optional) _____

U.S. Citizen? _____ Yes _____ No

Have you ever been a member of the AARC? _____

If so, when? From _____ to _____

Preferred mailing address: ☐ Home ☐ Business

For office use only

FOR ACTIVE MEMBER

An individual is eligible if he/she lives in the U.S. or its territories or was an Active Member prior to moving outside its borders or territories, and meets ONE of the following criteria: (1) is legally credentialed as a respiratory care professional if employed in a state that mandates such, OR (2) is a graduate of an accredited educational program in respiratory care, OR (3) holds a credential issued by the NBRC. An individual who is an AARC Active Member in good standing on December 8, 1994, will continue as such provided his/her membership remains in good standing.

PLEASE USE THE ADDRESS OF THE LOCATION WHERE YOU PERFORM YOUR JOB, NOT THE CORPORATE HEADQUARTERS IF IT IS LOCATED ELSEWHERE.

Place of Employment _____

Address _____

City _____

State _____ Zip __ __ __ __ __ - __ __ __ __

Phone No. (_____) _____

Medical Director/Medical Sponsor _____

FOR ASSOCIATE OR SPECIAL MEMBER

Individuals who hold a position related to respiratory care but do not meet the requirements of Active Member shall be Associate Members. They have all the rights and benefits of the Association except to hold office, vote, or serve as chair of a standing committee. The following subclasses of Associate Membership are available: Foreign, Physician, and Industrial (individuals whose primary occupation is directly or indirectly devoted to the manufacture, sale, or distribution of respiratory care equipment or supplies). Special Members are those not working in a respiratory care-related field.

PLEASE USE THE ADDRESS OF THE LOCATION WHERE YOU PERFORM YOUR JOB, NOT THE CORPORATE HEADQUARTERS IF IT IS LOCATED ELSEWHERE.

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State _____ Zip __ __ __ __ __ - __ __ __ __

Phone No. (_____) _____

FOR STUDENT MEMBER

Individuals will be classified as Student Members if they meet all the requirements for Associate Membership and are enrolled in an educational program in respiratory care accredited by, or in the process of seeking accreditation from, an AARC-recognized agency.

SPECIAL NOTICE — Student Members do not receive Continuing Respiratory Care Education (CRCE) transcripts. Upon completion of your respiratory care education, continuing education credits may be pursued upon your reclassification to Active or Associate Member.

School/RC Program _____

Address _____

City _____

State _____ Zip __ __ __ __ __ - __ __ __ __

Phone No. (_____) _____

Length of program

- ☐ 1 year
- ☐ 2 years
- ☐ 4 years
- ☐ Other, specify _____

Expected Date of Graduation (REQUIRED INFORMATION)

Month _____ Year _____

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American Association for Respiratory Care Membership Application

Demographic Questions

We request that you answer these questions in order to help us design services and programs to meet your needs.

Check the Highest Degree Earned

- ☐ High School
- ☐ RC Graduate Technician
- ☐ Associate Degree
- ☐ Bachelor's Degree
- ☐ Master's Degree
- ☐ Doctorate Degree

Number of Years in Respiratory Care

- ☐ 0-2 years
- ☐ 3-5 years
- ☐ 6-10 years
- ☐ 11-15 Years
- ☐ 16 years or more

Job Status

- ☐ Full Time
- ☐ Part Time

Credentials

- ☐ RRT
- ☐ CRTT
- ☐ Physician
- ☐ CRNA
- ☐ RN
- ☐ LVN/LPN
- ☐ CPFT
- ☐ RPFT
- ☐ Perinatal/Pediatric

Salary

- ☐ Less than $10,000
- ☐ $10,001-$20,000
- ☐ $20,001-$30,000
- ☐ $30,001-$40,000
- ☐ $40,000 or more

PLEASE SIGN

I hereby apply for membership in the American Association for Respiratory Care and have enclosed my dues. If approved for membership in the AARC, I will abide by its bylaws and professional code of ethics. I authorize investigation of all statements contained herein and understand that misrepresentations or omissions of facts called for is cause for rejection or expulsion.

A yearly subscription to RESPIRATORY CARE journal and *AARC Times* magazine includes an allocation of $6.50 from my dues for each of these publications.

NOTE: Contributions or gifts to the AARC are not tax deductible as charitable contributions for income tax purposes. However, they may be tax deductible as ordinary and necessary business expenses subject to restrictions imposed as a result of association lobbying activities. The AARC estimates that the nondeductible portion of your dues — the portion which is allocable to lobbying — is 26%.

Signature _____

Date _____

Membership Fees

Payment must accompany your application to the AARC. Fees are for 12 months. (NOTE: Renewal fees are $65.00 Active, Associate-Industrial or Associate-Physician, or Special status; $80.00 for Associate-Foreign status; and $35.00 for Student status).

☐ Active	$77.50
☐ Associate (Industrial or Physician)	$77.50
☐ Associate (Foreign)	$92.50
☐ Special	$77.50
☐ Student	$35.00
TOTAL	$_____

Specialty Sections

Established to recognize the specialty areas of respiratory care, these sections publish a newsletter four times a year that focuses on issues of specific concern to that specialty. The sections also design the specialty programming at the national AARC meetings.

☐ Adult Acute Care Section	$5.00
☐ Education Section	$10.00
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☐ Transport Section	$5.00
☐ Home Care Section	$5.00
☐ Subacute Care Section	$5.00
TOTAL	$_____

GRAND TOTAL = Membership Fee plus optional sections **$**_____

- ☐ Total Amount Enclosed $_____
- ☐ Please charge my dues (see below)

To charge your dues, complete the following:

- ☐ MasterCard
- ☐ Visa

Card Number

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Signature _____

Mail application and appropriate fees to:
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Relationship between Chronic Dyspnea and Expiratory Flow Limitation in Patients with Chronic Obstructive Pulmonary Disease—L Eltayara, MR Becklake, CA Volta, J Milic-Emili. Am J Respir Crit Care Med 1996;154:1726.

The purpose of this study was to assess whether expiratory flow limitation (FL), as measured by applying negative pressure at the mouth during tidal expiration, is a better predictor of dyspnea than routine spirometry measurements. The study population consisted of 117 ambulatory patients with COPD. Dyspnea was assessed according to the ATS-DLD respiratory Questionnaire. Expiratory flow limitation was measured in supine and sitting positions, and expressed as a percentage of the expired control tidal volume affected by flow limitation (FL, % V_T). Using Spearman's rank correlation (r_s), we found that the correlation of dyspnea scale with FL was stronger ($r_s > 0.5$) than with FVC ($r_s < -0.3$) or FEV_1 ($r_s < -0.4$) in both positions. In a multiple regression analysis FL remained the best predictor of dyspnea scale even after adjustment for FEV_1 (% predicted). Finally, FL was almost as sensitive as FEV_1 (% predicted) but much more specific in assessing the severity of dyspnea scale. These findings suggest that expiratory flow limitation as measured by the negative expiratory pressure technique may be more useful in the evaluation of dyspnea in patients with COPD than spirometry measurements.

Increasing Incidence of Withholding and Withdrawal of Life Support from the Critically Ill—TJ Prendergast, JM Luce. Am J Respir Crit Care Med 1997;155:15.

To determine whether limits to life-sustaining care are becoming more common, we attempted to quantify the incidence of recommendations to withhold or withdraw life support from critically ill patients, to describe how patients respond to these recommendations, and to examine how conflicts over these recommendations are resolved. In 1992 and 1993 we prospectively enrolled 179 consecutive patients from 2 intensive care units (ICUs) for whom a recommendation was made to withhold or withdraw life support. Where possible, we compared results with data collected in the same units over a similar time period in 1987 and 1988. Recommendations to withhold or withdraw life support preceded 179 of 200 deaths (90%) in 1992 and 1993, compared with 114 of 224 deaths (51%) in 1987 and 1988 ($\chi^2 = 73.76$, $p < 0.001$). Cardiopulmonary resuscitation was initiated in 10% of deaths in 1992 and 1993 as compared with 49% in 1987 and 1988. Ninety percent of patients agreed within less than 5 days, and only 8 patients (4%) refused physicians' recommendations to limit life support. In cases of conflict, physicians in 1992 and 1993 deferred to patients with one exception: physicians were willing to refuse surrogate requests for resuscitation of patients they considered hopelessly ill. We conclude that 90% of patients who die in these ICUs now do so following a decision to limit therapy, that this represents a major change in practice in these institutions over a period of 5 years, that most patients and surrogates accept an appropriate recommendation to withhold or withdraw life support, and that physicians will refuse surrogate requests in certain circumstances. *See the related editorial:* ***Managing Death and Dying in the Intensive Care Unit****—JHT Karlawish, JB Hall. Am J Respir Crit Care Med 1997;155:1-2.*

Intensive Care of Patients with HIV Infection: Utilization, Critical Illnesses, and Outcomes. MJ Rosen, K Clayton, RF Schneider, W Fulkerson, AV Rao, J Stansell, et al, and The Pulmonary Complications of HIV Infection Study Group. Am J Respir Crit Care Med 1997;155:67.

To examine intensive care unit (ICU) admission rates and diagnoses of patients with HIV infection, and to determine the outcomes of different critical illnesses, we analyzed data derived from the 63 patients who were admitted to an ICU from among the 1,130 adults with HIV infection who did not have AIDS at the time of enrollment in a multicenter prospective study. Patients were admitted and treated according to the judgment of their physicians. During 4,298 patient-years of follow-up for the entire cohort, there were 1,320 hospital admissions, of which 68 (5%) included admission to an ICU. Twenty-five (40%) of the patients admitted to the ICU died during that admission. Twenty-four patients (38%) were admitted with a principal diagnosis of lung disease; 11 had *Pneumocystis carinii* pneumonia (PCP), 1 of whom was coinfected with *Aspergillus fumigatus* and *Legionella pneumophilia*, and 6 of them (55%) died. Four had bacterial pneumonia, 2 had pulmonary edema caused by renal failure, and 1 each had pulmonary tuberculosis, pulmonary Kaposi's sarcoma, pneumothorax, adult respiratory distress syndrome, severe pulmonary fibrosis, cytomegalovirus pneumonitis, and metastatic adenocarcinoma to the lungs. Eleven of these 14 patients (79%) died. Thirty-nine patients had 44 admissions for nonpulmonary diagnoses, including gastrointestinal disorders (14 admissions), cardiovascular disorders (9), sepsis syndrome (6), neurologic disorders (4), monitoring and ICU nursing care during or after a procedure (4), metabolic disorders (3), trauma (2), drug overdose (1), and unknown reasons (1). Nine (23%) of these patients died. Twenty-eight patients underwent mechanical ventilation, and 16 (57%) died. Seven (25%) had PCP (5 died), 7 had other primary pulmonary diseases (6 died), and 14 were placed on mechanical ventilation for nonpulmonary disorders (5 died). Survival did not correlate with CD4 count determined within 6 months of admission to the ICU. In conclusion, the range of indications for critical care in patients with HIV infection is diverse. PCP accounted for only 16% of the ICU admissions, and mechanical ventilation for PCP and other pulmonary disorders was associated with a high mortality rate. In contrast, mechanical ventilation for nonpulmonary disorders, and admission to the ICU for nonpulmonary diagnoses was associated with a more favorable outcome.

Lower Respiratory Illness, Recurrent Wheezing, and Day Care Attendance—MC Marbury, G Maldonado, L Waller. Am J Respir Crit Care Med 1997;155:156.

We prospectively assessed the relations between various characteristics of day care and lower respiratory illness (LRI) in a cohort of 1,268 Minnesotan children, born between October 1989 and January 1991 and followed to 2 years of age. Information on LRI was abstracted from medical records and data on day care use, respiratory symptoms, and physician diagnosis of asthma were obtained from questionnaires. We identified a subgroup of 60 children with recurrent wheezing illnesses. The LRI rate ratio for day care attendance was 2.0 (95% confidence interval = 1.7, 2.2). Rate ratios were similar regardless of the day care setting, number of other children present, or the number of hours spent in day care. A parental history of asthma further increased the rate ratio for day care attendance. Day care attendance was associated with a 3-fold risk of having recurrent wheezing illnesses. We conclude that day care attendance is an important risk factor for LRI in young children, and for recurrent wheezing illnesses.

Racial Differences in Sleep-Disordered Breathing in African-Americans and Caucasians—S Redline, PV Tishler, MG Hans, TD Tosteson, KP Strohl, K Spry. Am J Respir Crit Care Med 1997:155:186.

In this case-control family study of sleep-disordered breathing (SDB), we describe the distributions of SDB and SDB risk factors in African-Americans and Caucasians. A total of 225 African-Americans and 622 Caucasians, ages 2 to 86 years, recruited as members of families with an individual with known sleep apnea (85 index families) or as members of neighborhood control families (63 families) were studied with an overnight home sleep-study, questionnaires, and physical measurements. A subsample underwent cephalometry. Outcome measures were the respiratory disturbance index (RDI) and a binary variable indicating the presence of increased apneic activity (IAA). In both races, a strong relationship was demonstrated between the (log transformed) RDI and age and age^2. African-Americans with SDB were younger than Caucasians with SDB (37.2 ± 19.5 vs 45.6 ± 18.7 yr, $p < 0.01$). In subjects ≤ 25 years, RDI level and IAA prevalence were higher in African-Americans (odds ratio, adjusted for obesity, sex, proband sampling, and familial clustering, 1.88, 1.03 to 3.52, 95% CI). In this age group, racial differences also were

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observed in the relationship between RDI and age ($p < 0.001$ for the RDI-age interaction). This suggests that young African-Americans may be at increased risk for sleep apnea.

Effects of Sleep Posture on Upper Airway Stability in Patients with Obstructive Sleep Apnea—AM Neill, SM Angus, D Sajkov, RD McEvoy. Am J Respir Crit Care Med 1997; 155:199.

Changes in sleep posture have been shown to improve obstructive sleep apnea (OSA). To investigate the mechanisms by which this occurs we assessed upper airway stability in 8 patients with severe OSA in 3 postures (supine, elevated to 30°, and lateral). We used a specially adapted nasal continuous positive airway pressure (nCPAP) mask to measure upper airway closing pressure (UACP) and upper airway opening pressure (UAOP) during non-REM sleep. Statistical comparisons were made between postures using ANOVA for repeated measures. Elevation resulted in a less collapsible airway compared with both the supine and lateral positions (mean UACP: 30° elevation -4.0 ± 3.2 compared with supine 0.3 ± 2.4 cm H_2O, $p < 0.05$ and; lateral -1.1 ± 2.2 cm H_2O, $p < 0.05$). Supine UACP and lateral UACP were not significantly different. Elevation or lateral positioning produced a 50% reduction in mean UAOP (supine 10.4 ± 3.5 cm H_2O compared with 30° elevation 5.3 ± 2.1, $p < 0.05$; and lateral 5.5 ± 2.1 cm H_2O, $p < 0.05$). We conclude that in severely affected OSA patients upper body elevation, and to a lesser extent lateral positioning, significantly improve upper airway stability during sleep, and may allow therapeutic levels of nCPAP to be substantially reduced.

Adjustment of DL_{CO} for Hemoglobin Concentration—RM Marrades, O Diaz, J Roca, JM Campistol, JV Torregrosa, JA Barberà, et al. Am J Respir Crit Care Med 1997;155:236.

The equation proposed by Cotes and coworkers is currently considered as the most acceptable to correct carbon monoxide diffusing capacity (DL_{CO}) for hemoglobin concentration [Hb] by both the American Thoracic Society (ATS) and the European Respiratory Society (ERS) guidelines for standardization of DL_{CO}. In a previous study on 24 anemic patients undergoing bone marrow transplantation (1), we found that DL_{CO} is underestimated using the equation of Cotes and coworkers. To further explore this finding, 28 anemic patients ([Hb] = 8.2 ± 1.0 (SD) g/dL) with chronic renal failure were prospectively studied during the recovery period of anemia (5.4 ± 3.5 mo). In all 28 subjects, the slope $\Delta DL_{CO}/\Delta[Hb]$ computed as ratio of overall change in DL_{CO} to overall change in [Hb] throughout the study period was 1.40 ± 0.72 mL CO/min/mm Hg/g/dL. The individual relationship between measured DL_{CO} and [Hb] closely fitted a simple linear regression. The resulting equations for adjustment of DL_{CO} (DL_{CO}adj) to a standard [Hb] of 14.6 g/dL for men and 13.4 g/dL for women are: DL_{CO}adj (men) = DL_{CO}obs + 1.40 (14.6 − [Hb]); and DL_{CO}adj (women) = DL_{CO}obs + 1.40 (13.4 − [Hb]). The present adjustment function for DL_{CO} is linear and independent of the observed DL_{CO} values, whereas the formulas previously proposed are curvilinear, DL_{CO} correction varying with the measured DL_{CO} values. For a measured DL_{CO} of 15 mL CO/min/mm Hg and [Hb] ranging from 7 to 12 g/dL, the present DL_{CO} adjustment is higher (by 2.7 mL CO/min/mm Hg, on average) than that proposed by Cotes and coworkers. This difference appears to be relevant for a precise interpretation of DL_{CO} in patients with normocytic anemia in different clinical conditions.

Spirometry Values in Stable Lung Transplant Recipients—JAB Martinez, IL Paradis, JH Dauber, W Grgurich, T Richards, SA Yousem, et al. Am J Respir Crit Care Med 1997;155:285.

To clarify the usefulness of pyrometry to assess the function of the lung allograft post-transplant, we retrospectively reviewed 351 sequential spirometry measurements performed by 65 healthy recipients after the 80th postoperative day when the clinical evaluation and fiberoptic bronchoscopy with transbronchial biopsies and bronchoalveolar lavage excluded significant rejection or infection in the allograft. The mean coefficients of variation (CV) and significant values for change (SC) for the FVC, FEV_1, and $FEF_{25-75\%}$ were calculated according to the type of transplant procedure (heart-lung and double-lung [HL-DL] vs single-lung [SL]), and to the time after transplant when the spirometry measurements were obtained (≤ 1 yr vs > 1 yr). The SC for the FVC decreased with time after transplantation for both HL-DL (≤ 1 yr: 17% vs > 1 yr: 7%) and SL recipients (≤ 1 yr: 13% vs > 1 yr: 8%). The higher degree of variability within the first year was primarily due to increasing values especially in the HL-DL recipients. The SC

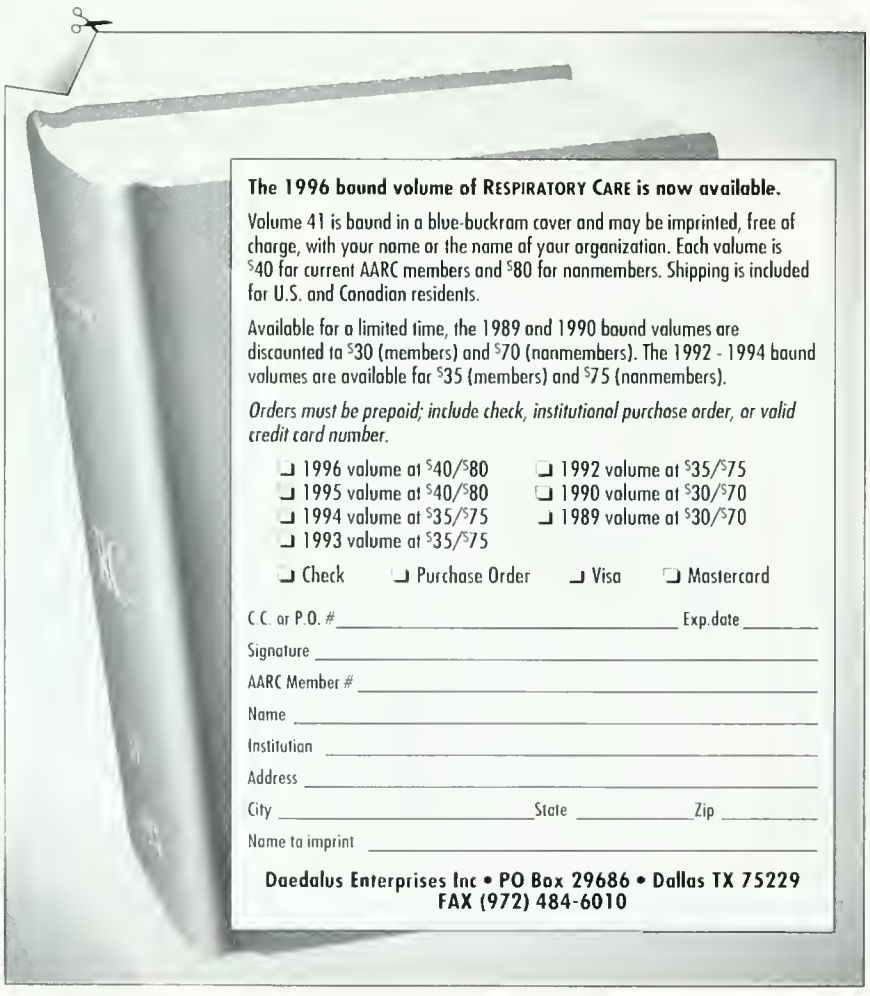
for the FEV_1 also decreased over time for HL-DL recipients (≤ 1 yr: 18% vs > 1 yr: 9%) but was similar for SL recipients at both intervals (13%). Our results suggest that decreases of ≥ 11% in FVC or 12% in FEV_1 in HL-DL recipients and ≥ 12% in FVC or 13% in FEV_1 for SL recipients indicate a significant decrease in allograft function that may be due to infection or rejection.

Prevention of Pediatric Drowning and Near-Drowning: A Survey of Members of the American Academy of Pediatrics—JE O'Flaherty, PL Pirie. Pediatrics 1997;99(2):169.

OBJECTIVE: To assess pediatricians' knowledge about the epidemiology of childhood drowning, their opinions and current practices regarding its prevention, and their interest in taking on more responsibility for its prevention. DESIGN: A self-administered questionnaire was mailed to 800 pediatricians in the United States, randomly selected from the American Academy of Pediatrics' approximately 18,000 full fellows. RESULTS: A total of 560 completed surveys were returned, a response rate of 70.1%. Although 85% of respondents believe it is the responsibility of pediatricians to become involved in community and/or legislative efforts to prevent childhood drowning, only 4.1% were involved in such efforts. Only a minority of respondents provided written materials and anticipatory guidance on drowning prevention to their patients. Women were more likely than men to discuss drowning prevention with their patients. Younger physicians were more likely than older physicians to discuss drowning prevention with their patients. Physicians who received formal education on drowning prevention during their pediatric residency training were more likely to provide written materials and anticipatory guidance on drowning prevention to their patients. However, only 17.9% of respondents received formal education on drowning prevention during their pediatric residency training. Seventy-four percent of all respondents felt that further education on the prevention of childhood drowning and near-drowning would be useful to them. CONCLUSION: Although drowning is the second leading cause of death by unintentional injury in the pediatric population (aged 0 to 19 years), most pediatricians do not routinely provide information to their patients, or to their patients' parents, on drowning prevention. IMPLICATION: Pediatricians have been effective child advocates in many areas of injury prevention. If the prevention of drowning is made a priority in pediatric practice, many more children's lives will be saved.

Improving Care for Minority Children with Asthma: Professional Education in Public Health Clinics—D Evans, R Mellins, K Lobach, C Ramos-Bonoan, M Pinkett-Heller, S Wiesemann, et al. Pediatrics 1997;99(2):157.

OBJECTIVE: Recent studies have shown that lack of continuing primary care for asthma is associated with increased levels of morbidity in low-income minority children. Although effective preventive therapy is available, many African-American and Latino children receive episodic treatment for asthma that does not follow current guidelines for care. To see if access, continuity, and quality of care could be improved in pediatric clinics serving low-income children in New York City, we trained staff in New York City Bureau of Child Health clinics to provide continuing, preventive care for asthma. METHODS: We evaluated the impact of the intervention over a 2-year period in a controlled study of 22 clinics. Training for intervention clinic staff was based on National Asthma Education and Prevention Program guidelines for the diagnosis and management of asthma, and included screening to identify new cases and health education to improve family management. The intervention included strong administrative support by the Bureau of Child Health to promote staff behavior change. We hypothesized that after the intervention, clinics that received the intervention would, compared with control clinics, have increased numbers of children with asthma receiving continuing care in the clinics and increased staff use of new pharmacologic and educational treatment methods. RESULTS: In both the first and second follow-up years, the intervention clinics had greater positive changes than control clinics on measures of access, continuity, and quality of care. For second year follow-up data these include: for access, greater rate of new asthma patients (40/1,000 vs 16/1,000; $p < 0.01$); for continuity, greater percentage of asthma patients returning for treatment 2 years in a row (42% vs 12%; $p < 0.001$) and greater annual frequency of scheduled visits for asthma/patient (1.85 vs 0.88; $p < 0.001$); and for quality, greater percentage of patients receiving inhaled β agonists (52% vs 15%; $p < 0.001$) and inhaled anti-inflammatory drugs (25% vs 2%; $p < 0.001$), and greater percentages of parents who reported receiving patient education on 12 topics from Bureau of Child Health physicians (71% vs 58%; $p < 0.01$) and nurses (61% vs 44%; $p < 0.05$). CONCLUSION: We conclude that the intervention substantially increased the Bureau of Child Health staff's ability to identify children with asthma, involve them in continuing care, and provide them with state-of-the-art care for asthma. *See the related editorial:* ***Improving Our Public Health System's Care for Chil-***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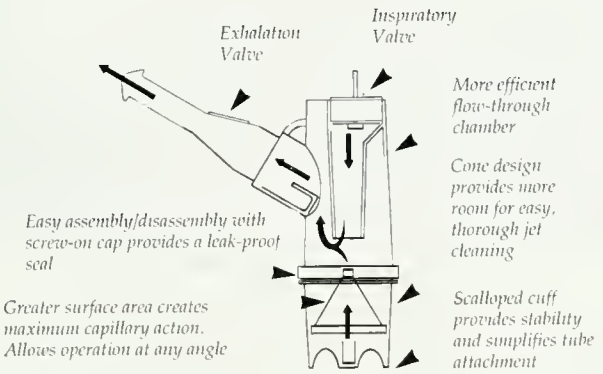
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IV. Asthma Disease Management: Using the Revised NAEPP Guidelines in Practice
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dren with Asthma—KB Weiss, WW Addington. Pediatrics 1997;99(2):252-254.

Hospital and Patient Characteristics Associated with Variation in 28-Day Mortality Rates for Very Low Birth Weight Infants—JD Horbar, GJ Badger, EM Lewit, J Rogowski, PH Shiono. Pediatrics 1997;99(2):149.

BACKGROUND: The outcomes for very low birthweight infants vary among neonatal intensive care units (NICUs), but the reasons for this variation are not well understood. We used the database of a large neonatology research network to determine whether either admission characteristics of the infants or specific characteristics of the units such as annual patient volume and the presence of a pediatric residency program could account for observed differences in neonatal mortality rates among units. METHODS: We studied 7,672 infants with birthweights from 501 to 1,500 g treated during 1991 and 1992 at 62 NICUs participating in the Vermont Oxford Network Database. RESULTS: Overall, 14.7% of the study infants died within 28 days of birth (interquartile range 9.9% to 18.1%). The ratio of the number of observed deaths at an NICU to the number of deaths predicted based on the characteristics of infants treated at the NICU (standardized neonatal mortality ratio, [SNMR]) varied significantly among units (range 0 to 1.69, $z = 4.24$). There was no association between annual patient volume and either mortality rate ($r = 0.17$) or SNMR ($r = 0.22$). Observed mortality rates (17% vs 13%) and SNMR (1.04 vs 0.87) were both higher at the 24 hospitals with pediatric residency training programs than at the 38 hospitals without such programs. Hospitals with residency programs had higher average annual patient volumes (104 vs 66). In an analysis simultaneously adjusting for patient characteristics, volume, and presence of a residency program, neither volume (odds ratio [OR] per 10 additional cases treated 1.01, 95% confidence interval [CI], 0.98 to 1.04) nor presence of a pediatric residency program (OR 1.18, 95% CI, 0.94 to 1.47) was significantly associated with neonatal mortality risk. CONCLUSION: There are differences in neonatal mortality rates among NICUs that cannot be explained by differences in the measured admission characteristics of the infants, suggesting that the effectiveness of medical care varies among units. Neither the annual volume of very low birthweight infants treated in a unit nor the presence of a pediatric residency training program was independently associated with neonatal mortality rates for very low birthweight infants. *See the related editorials:* ***Quality of Care: An Overdue Agenda****—MC McCormick, Pediatrics 1997;99(2):249-250; and* ***Data From Randomized Trial Networks: When Less Is More****—MB Bracken. Pediatrics 1997;99(2):250-252.*

Children and Adult Perceptions of Childhood Asthma—GH Guyatt, EF Juniper, LE Griffith, DH Feeny, PJ Ferrie. Pediatrics 1997;99(2):165.

OBJECTIVE: To explore children's and parents' assessment of children's asthma. DESIGN: Prospective 2-month cohort study in which children and parents were reviewed at baseline and 1-month intervals. SETTING: Mid-sized, English-speaking, industrial community serving an urban and regional rural population. PATIENTS OR PARTICIPANTS: Fifty-two children, 7 to 17 years old, with a wide range of asthma severity, and their parents. INTERVENTIONS: We offered patients with inadequately controlled asthma additional inhaled steroid. MAIN OUTCOME MEASURES: Children and parents provided global ratings of change in childhood symptoms and children completed spirometry and the Paediatric Asthma Quality of Life Questionnaire at clinic visits. Patients recorded peak flow rates, symptoms, and medication use in a daily diary. The diary symptom report, medication use, and spirometry were combined to form an asthma control score. RESULTS:

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In children younger than 11, children's global rating of change in symptoms correlated strongly with changes in quality of life (0.54 to 0.67) but not with measures of airway caliber or asthma control, while parents' global ratings did not correlate with children's quality of life but showed moderate correlations with airway caliber (0.29 to 0.48) and asthma control (0.50). In children over the age of 11, correlations with all clinical variables were higher for their own than their parents' global ratings. CONCLUSIONS: In children under 11, clinicians can gain complementary information from questioning children and parents. For children over 11, parents can provide little if any information beyond that obtained through questioning the child.

The Influence of Physician Explanations on Patient Preferences about Future Health-Care States—DJ Mazur, DH Hickam. Med Decis Making 1997;17:56.

OBJECTIVE: To determine the influence of alternative explanations by physicians of the purpose of a medical intervention (intubation and ventilatory support, IVS) on 3 types of patient preferences: desire for IVS, the length of time patients would find IVS acceptable, and the minimum probability of a good medical outcome patients would require before assenting to continued support with IVS. METHODS: Structured interviews were conducted with patients followed in a continuity care general medicine clinic at the Department of Veterans Affairs Medical Center, Portland, Oregon. Patients were asked to consider whether they would accept IVS at a future time. Patients were randomly assigned to 1 of 2 explanation conditions that differed in terms of their future medical contexts, that is, the degrees of specification of the nature of the medical condition patients were asked to consider. The general-explanation group was asked to consider the future medical context of "an unspecified medical condition"; the specific-explanation group was asked to consider the future medical context of "a severe pneumonia." Patients were asked 3 questions: (1) Would you accept IVS (yes or no)? (2) How long would you allow your physician to continue IVS?; and (3) After being on IVS for 2-3 days, what would be the minimum chance of recovery from the condition you would require before agreeing to continued IVS? "Chance of recovery" was defined for both groups as the probability that the patient would be able to leave the hospital and be able to take care of activities of daily living unassisted with minimal change in his or her mental state from the prehospitalization status. RESULTS: Of 186 patients (mean age = 66.5 years; mean education = 12.7 years), 97 received the general explanation and 89 received the specific explanation about a severe pneumonia. Significantly fewer ($p = 0.03$) patients receiving the general explanation wanted physicians to intervene with IVS (general 94% vs specific 100%). Patients receiving the general explanation were willing to accept significantly fewer ($p = 0.009$) days of intubation (general 65 days vs specific 96 days). Significantly fewer ($p < 0.0001$) patients receiving the general explanation wanted physicians to continue IVS when the probability of a successful outcome was less than 50% (general 30% vs specific 64%). CONCLUSION: Physician explanations—based on general (unspecified medical condition) vs specific (severe pneumonia) explanations—have a marked influence on the duration of IVS patients would permit and the probability of a good outcome required to continue IVS.

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Predicting Difficult Intubation with Indirect Laryngoscopy—K Yamamoto, T Tsubokawa, K Shibata, S Ohmura, S Nitta, T Kobayashi. Anesthesiology 1997;86(2):316.

BACKGROUND: It is not always possible to predict when tracheal intubation will be difficult or impossible. The authors wanted to determine whether indirect laryngoscopy could identify patients in whom intubation was difficult. METHODS: Indirect laryngoscopy was done in 2,504 patients. The Wilson risk sum score and the modified Mallampati score were also studied in a different series of 3,680 patients for comparison. These predictive methods were compared according to 3 parameters: positive predictive value, sensitivity, and specificity. RESULTS: Of 6,184 patients studied, the trachea proved difficult to intubate in 82 (1.3%). Positive predictive value (31%) and specificity (98.4%) with indirect laryngoscopy were greater than the other 2 predictive methods ($p < 0.01$), whereas sensitivity with indirect laryngoscopy (69.2%) was greater than that of the Wilson risk sum score (55.4%) ($p < 0.01$). CONCLUSIONS: Although in 15% of patients indirect laryngoscopy could not be performed because of excessive gag reflex, indirect laryngoscopy can serve as an effective method to predict difficult intubation.

Hypoxic Pulmonary Vasoconstriction in Human Lungs: A Stimulus-Response Study—K Hambraeus-Jonzon, L Bindslev, ÅJ Mellgård, G Hedenstierna. Anesthesiology 1997;86(2):308.

BACKGROUND: A stimulus-response relation between alveolar oxygen tension and pulmonary vascular resistance has been observed in animals. This study investigated this relation in healthy human lungs. The distribution of pulmonary blood flow was measured during unilateral (1) graded hypoxia (fractional concentration of oxygen in inspired gas [F_{IO_2}] = 0.12, 0.08, and 0.05) and contralateral hyperoxia ($F_{IO_2} = 1.0$; $n = 6$); (2) single-step hypoxia ($F_{IO_2} = 0.05$) and contralateral hyperoxia ($n = 5$); and (3) normobaric hyperoxia and contralateral normoxia ($F_{IO_2} = 0.25$; $n = 6$). METHODS: Seventeen patients with healthy lungs were studied during intravenous anesthesia. The lungs were separately and synchronously ventilated. The relative perfusion of each lung was assessed by the inert gas (sulfurhexafluoride) elimination technique. RESULTS: (1) Unilateral graded hypoxia reduced the perfusion of the hypoxic lung from a mean (±SD) of 52 (2)% of cardiac output ($\dot{Q}$) during bilateral hyperoxia, to 47 (5)% ($p > 0.05$), 40 (3)% ($p < 0.01$), and 30 (8)% ($p < 0.001$) of $\dot{Q}$, respectively. These progressive reductions in the perfusion of the hypoxic lung were all significantly different from each other. (2) Unilateral single-step hypoxia caused a blood flow diversion of the same magnitude as when the lung was previously ventilated with F_{IO_2} of 0.12 and 0.08. The perfusion of the hypoxic lung was reduced from 46 (9)% of $\dot{Q}$ (bilateral hyperoxia), to 26 (4)% of $\dot{Q}$ ($p < 0.01$). (3) Unilateral hyperoxia did not significantly change the relative blood flow distribution between the 2 lungs or the pulmonary artery pressure. CONCLUSIONS: A stimulus-response relation between graded hypoxia and blood flow diversion defines hypoxic pulmonary vasoconstriction in the normal human lung. Hyperoxia has no significant effect on vascular resistance in the normal human lung.

Dilutional Acidosis: Is It a Real Clinical Entity?—DD Mathes, RC Morell, MS Rohr. Anesthesiology 1997;86(2):501.

Dilutional acidosis occurs as a result of rapid extracellular volume expansion decreasing the measured serum bicarbonate. This phenomenon is not well described in the literature. Searching the English medical literature, we found only 1 case report of dilutional acidosis and no case reports of dilutional acidosis occurring within the perioperative period. Several authors have concluded that dilutional acidosis has little actual clinical significance because of cellular buffering in which rapid extracellular volume expansion causes only minimal changes in measured extracellular bicarbonate and pH levels. We report a case of dilutional acidosis occurring intraoperatively as a direct result of giving a large volume of isotonic saline.

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Consensus Conference IV: Noninvasive Positive Pressure Ventilation

A Special Issue

containing the papers and Consensus Statement from
the Conference held October 4-6, 1996, in Vail, Colorado

This Conference was made possible by educational grants to the American Respiratory Care Foundation

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Consensus Conference: Noninvasive Positive Pressure Ventilation

Preamble

Objectives

The Consensus Conference on Noninvasive Positive Pressure Ventilation (NPPV) was convened on October 4-6, 1996, by the American Association for Respiratory Care, the American Respiratory Care Foundation, and RESPIRATORY CARE Journal to address (1) the terminology of NPPV, (2) the clinical situations in which the use of NPPV may be appropriate, (3) desirable design and performance characteristics of devices for delivering NPPV, (4) important aspects of the clinical application of this form of ventilatory support, and (5) the aspects about which further study would be most useful.

The conveners believe that a consensus conference on NPPV was needed because of (1) the rapid increase in both published experience and the clinical use of NPPV in the last several years, and (2) the confusion that has resulted from inconsistent terminology, applications for different patient diagnoses, diverse clinical settings, and the use of different devices and ventilation techniques.

NPPV was defined as **the application of positive pressure via the upper respiratory tract for the purpose of augmenting alveolar ventilation**. The following aspects were not addressed specifically at the Conference and do not appear in this consensus document: (1) application of positive pressure to areas of the body other than the upper respiratory tract, as with intermittent abdominal pressure ventilation; (2) application of positive pressure ventilation via an endotracheal or tracheostomy tube; (3) continuous positive airway pressure (CPAP) without additional inspiratory assistance; (4) intermittent positive pressure breathing (IPPB) given for the purpose of preventing or treating atelectasis in spontaneously breathing patients or for aerosol delivery; and (5) negative pressure ventilation.

Presenters

Eleven presenters were selected by the Conference Chairmen based on their interest and expertise in NPPV. Additional discussants were nominated by Conference sponsors.

Evidence

At the Conference, formal presentations on different aspects of NPPV by the invited speakers were given and appear in the April 1997 issue of RESPIRATORY CARE [Respir Care 1997;42(4)].

Consensus Process

Prior to the Conference, an outline of the Conference goals was prepared by the co-chairs and circulated to the participants. Strength of evidence was judged using an established schema (Table 1). Following presentations and discussion, the Writing Committee met on-site and prepared an initial Consensus Statement based on the presentations and discussion. The Statement was presented to all participants for discussion and suggested revision on the last morning of the Conference. A revised draft was then prepared by the Writing Committee and circulated to all participants prior to final editing and publication. Unless otherwise noted, statements and recommendations represent unanimous agreement.

Table 1. Levels of Evidence for Evaluating NPPV*

Level I: Randomized controlled trials (RCTs) with low false-positive and false-negative errors
Level II: RCTs with high false-positive and false-negative errors
Level III: Nonrandomized, concurrent-cohort comparisons
Level IV: Nonrandomized, historical-cohort comparisons
Level V: Case series without control subjects

*Adapted from the American College of Chest Physicians project on "evidence-based medicine." (Cook DJ et al. Chest 1992;102:305S-311S)

Recommendations

After weighing the evidence, recommendations were made regarding: (1) patient populations and clinical settings, (2) characteristics of NPPV devices, (3) the NPPV ventilator approaches and techniques, and (4) the NPPV ventilator-patient interfaces employed.

Consensus Statement: Noninvasive Positive Pressure Ventilation

I. Terminology for NPPV

Considerable confusion can result from the use of imprecise terminology. In the NPPV literature, contradictory and ambiguous terms and abbreviations abound. Conference participants defined terms for use in discussing NPPV, making them consistent to the extent possible with the ARCF-AARC Consensus Statement on the Essentials of Mechanical Ventilators [Respir Care 1992;37(9):1000-1008].

Inspiratory Pressure. Positive airway pressure applied during inspiration. During volume-targeted ventilation, this pressure is a consequence of the set tidal volume and lung mechanics. During pressure-targeted ventilation, the level is clinician set. In some pressure-targeted devices, this setting is the absolute inspiratory pressure (ie, expiratory pressure is included, so-called "inspiratory positive airway pressure," or IPAP), whereas in other pressure-targeted devices this setting is the inspiratory pressure *above* expiratory pressure. The meaning of inspiratory pressure must be specified for each device.

Expiratory Pressure. Airway pressure during expiration. When this pressure is above atmospheric, it is termed positive end-expiratory pressure, or PEEP. This is synonymous with expiratory positive airway pressure, or EPAP.

NPPV-Delivered Breaths. Tidal breaths delivered by NPPV can be described by what triggers the breath (the trigger variable), what governs gas flow (the limit variable), and what terminates the breath (the cycle variable).

Commonly used breath types are:

- patient-triggered, pressure-limited, flow-cycled ('pressure support')
- patient-triggered, pressure-limited, time-cycled ('pressure-assist')
- machine-triggered, pressure-limited, time-cycled ('pressure control')
- patient-triggered, flow-limited, volume-cycled ('volume-assist')
- machine-triggered, flow-limited, volume-cycled ('volume control')

All of these breaths can be used with or without expiratory pressure. Strictly speaking, NPPV with PEEP provides 'bi-level positive airway pressure.' However, this term is sometimes used in a more restricted sense to describe NPPV that delivers 'pressure support' breaths with PEEP.

Constant (Continuous) Positive Airway Pressure (CPAP). Application of constant positive pressure (ie, above atmospheric pressure) throughout the ventilatory cycle. With CPAP, machine-delivered inspiratory pressure = expiratory pressure; and, thus, no inspiratory assistance is provided.

II. Clinical Issues

Goals for NPPV. Clinical situations in which NPPV has been evaluated and may be appropriate extend from settings in which acute resuscitative support is provided (ie, emergency room, intensive care unit, and postanesthesia care unit, or recovery room) to settings in which patients use NPPV as a long-term, regular treatment (ie, in an extended care facility or in the home). In these various settings, NPPV is used for one of two different treatment goals: (1) Type-1 support, the application of NPPV in a condition in which cessation of ventilatory support could lead to imminent death and (2) Type-2 support, the application of NPPV in a condition in which ventilatory support may confer clinical benefit (eg, providing ventilatory muscle rest or lowering P_{aCO_2}) but in which cessation of NPPV does not pose an immediate life-threatening risk. Evidence exists to support the use of both Type-1 and Type-2 NPPV. This evidence is briefly reviewed in the context of a proposed schema that delineates the strength of the clinical evidence (Table 1) and is summarized in Table 2.

Type-1 Ventilatory Support Applications. In the setting of acute respiratory failure, patients undergo ventilation to treat life-threatening hypoxemia and/or hypercapnia. Although the traditional treatment strategy for such patients has been to perform endotracheal intubation and initiate positive pressure ventilation, recent literature contains many examples in which NPPV has been applied successfully for patients with hypoxic and/or hypercapnic respiratory failure (eg, due to acute exacerbations of chronic obstructive pulmonary disease, or COPD; pneumonia; congestive heart failure; asthma; post-extubation respiratory failure; cystic fibrosis; decompensation in neuromuscular disease; and postoperative respiratory failure). Clinical case series and several prospective, randomized, controlled clinical trials demonstrate that NPPV can successfully support patients with acute respiratory failure and avert the need for endotracheal intubation in 50 to 75% of candidates. Evidence is particularly strong that NPPV may be successfully applied in patients with acute exacerbations of COPD (Table 2). Other reported outcomes in randomized, controlled trials have included lower mortality in NPPV subjects and shortened length of hospital stay without the need for increased health care provider attention.

It is recognized that NPPV is currently used in other acute circumstances (eg, hypoxic respiratory failure not associated with hypercapnia) but available evidence is less solid in establishing efficacy in these settings (Table 2). Selection an

Table 2. Summary of Current Conclusions Regarding the Use of NPPV and Types of Supportive Evidence*

Underlying Disease	For Type-1 Support†	Level of Evidence	For Type-2 Support†	Level of Evidence
Adult				
COPD	Effective to avert endotracheal intubation	I	May be effective	I (discordant results of RCTs)
	May decrease mortality	I		
	May shorten length of stay	I		
Asthma	May avert endotracheal intubation	III		
Other parenchymal lung disease	May be effective	II	May be effective	V
Cardiogenic pulmonary edema	Effective‡	I	—	—
Neuromuscular & chest-wall disease	Effective	III	Effective	III
Sleep-disordered breathing	—	—	CPAP effective, NPPV may be effective if CPAP fails	II
Pediatric				
Parenchymal lung disease (eg, acute pneumonia with hypoxemia)	May be effective	V	May be effective	V
Neuromuscular and chest-wall disease	May be effective	V	May be effective	V
Cystic fibrosis	May be effective	V	May be effective	V

*Rules of evidence adopted from Cook DJ, Guyatt GH, Laupacis A, Sackett DL. Chest 1992;102(4) (suppl):305S-311S

†Type-1 support = support for a condition in which cessation of ventilation could lead to imminent death; Type-2 support = support for a condition in which support may confer clinical benefit but cessation is not life threatening.

‡Although P_{aCO_2} was reduced by NPPV, a recent study shows an increase in the extension of myocardial infarction in the treated group.

exclusion criteria in patients in acute respiratory failure needing Type-1 support are listed in Table 3.

Once NPPV has been initiated, close observation is required to assess efficacy. Rapid improvement (ie, within 1 to 2 hours) in patient comfort (ie, reduced dyspnea, decreased respiratory rate, decreased use of accessory muscles, and/or synchronization with NPPV) and improvement of P_{aCO_2} and respiratory acidosis indicate success. Criteria for stopping attempts at NPPV and instituting alternative therapies include worsened encephalopathy or agitation, inability to clear secretions, inability to accept any of the interfaces tried, hemodynamic instability, or worsened oxygenation. Pulse oximetry and clinical assessment may indicate effective NPPV even if an elevated P_{aCO_2} does not fall. However, progressive hypercapnia in the face of NPPV indicates failure. While not contraindications to a trial of NPPV for Type-1 support, clinical features predicting lower likelihood of NPPV success include more severe illness (eg, high

Table 3. Selection and Exclusion Criteria for Candidates for Type-1 NPPV

Selection Criteria (at least 2 should be present)	Exclusion Criteria (any may be present)
Absolute	**Absolute**
Respiratory distress with moderate-to-severe dyspnea, use of accessory muscles of respiration, abdominal paradox	Respiratory arrest
pH < 7.35 with P_{aCO_2} > 45 torr	Cardiorespiratory instability (eg, hypotension with impaired perfusion, serious dysrhythmia, myocardial infarction with pulmonary edema*)
Respiratory rate ≥ 25/min (adults)	Uncooperative patient
	Recent facial, esophageal, or gastric surgery
	Craniofacial trauma or burns
	High aspiration risk (inability to manage secretions)
	Inability to protect airway
	Fixed anatomic abnormalities of the nasopharynx (eg, choanal atresia, severe laryngomalacia)
	Relative
	Extreme anxiety
	Massive obesity
	Copious secretions
	Acute respiratory distress syndrome (ARDS) as etiology of acute respiratory failure

*Although P_{aCO_2} was reduced by NPPV, a recent study shows an increase in the extension of myocardial infarction in the treated group.

APACHE score), presence of pneumonia or excessive secretions, or a large mouth leak.

In general, NPPV for acute respiratory failure should be used in a setting that offers close monitoring and the capability to initiate alternative support (eg, endotracheal intubation and other acute resuscitative measures) when necessary. Unless such capabilities exist (as in a dedicated step-down unit or special respiratory ward), an ICU or emergency room is the preferred clinical venue. Nevertheless, it is conceivable that stable patients who are being weaned from Level-1 NPPV can be managed on a general care hospital floor. Monitoring is critical under these circumstances and personnel well trained in NPPV techniques must be present. It is also conceivable that acute respiratory failure may develop in a patient on a general hospital floor, and NPPV may need to be applied while transfer to an ICU or other special care unit is being arranged.

NPPV is also used for long-term Type-1 support in individuals who are not acutely ill. Patients receiving chronic Type-1 support may reside in extended care facilities or, under special circumstances, at home. In specialized units dedicated to care of patients with neuromuscular disease, NPPV has been successfully used to continue ventilatory support as patients with tracheostomies are decannulated.

Type-2 Ventilatory Support Applications. In contrast to the use of NPPV in Type-1 support where current recommendations favor use in a relatively small subset of patients with acute respiratory failure (Table 2) and in closely monitored settings, the use of NPPV for Type-2 support has been described in a broader range of clinical conditions and a wider array of clinical settings. For patients with stable, hypercapnic COPD, 4 controlled trials (as of early 1997) have studied the efficacy of nocturnal application of NPPV. Of these, 1 study suggests benefit (ie, improved daytime gas exchange, enhanced quality of life and sleep quality), but the other 3 studies fail to show these benefits. Thus, the role of nocturnal NPPV in this setting is unclear and requires further study.

Other clinical conditions for which Type-2 NPPV has reported benefits (although with generally less rigorous evidence, Table 2) include progressive respiratory failure accompanying neuromuscular disease (eg, muscular dystrophies, post-polio syndrome, multiple sclerosis, amyotrophic lateral sclerosis), and chest-wall deformity (eg, kyphoscoliosis, post-thoracoplasty). Clinical case series also report successful use in patients with obesity hypoventilation and idiopathic hypoventilation. NPPV has been reported to be helpful in patients with obstructive sleep apnea who do not tolerate CPAP alone, but supportive controlled clinical trials are lacking. Other promising, albeit inadequately studied, clinical settings for use of NPPV in elective care include support of end-stage cystic fibrosis as a bridge to lung transplantation. Further study of these applications is required before NPPV can be endorsed.

When used as Type-2 support, NPPV is usually applied non-continuously (eg, nocturnally). Available reports clearly show that NPPV can be successfully initiated in intensive care, intermediate care settings (eg, regular nursing wards and subacute care facilities), and outpatient settings.

In considering NPPV for elective care, relative contraindications include severe upper airway dysfunction, copious secretions that cannot be cleared by spontaneous or assisted cough, or high oxygen requirements (ie, $F_{IO_2} \geq 0.40$). As with using NPPV in Type-1 support, successful use requires a cooperative and motivated patient.

Complications Associated with NPPV. Complications associated with the use of NPPV include leaks that compromise ventilation, mask discomfort, skin breakdown, eye irritation, sinus congestion, oronasal drying, and patient-ventilator dyssynchrony. Gastric insufflation is common although rarely of clinical significance. Lower inflation pressures may reduce this, and routine nasogastric-tube placement is not necessary. It is important to assure adequate cough and secretion clearance with NPPV. As with invasive mechanical ventilation, NPPV can impair cardiac filling and reduce cardiac output and blood pressure. Pneumothoraces and pneumonias also occur during NPPV but may be less common than with invasive mechanical ventilation.

III. Performance Characteristics for NPPV Devices

Performance characteristics required for NPPV devices differ depending upon the clinical situations described above. Performance characteristics under Type-1 and Type-2 ventilatory support conditions for which consensus was reached are given in Table 4.

IV. Aspects of NPPV Application That Clinicians Should Consider

A. Choice of Interface. Either a nasal mask or a full face mask is usually used for NPPV during acute respiratory failure, and published studies have reported success with both. For noninvasive ventilation in patients with chronic ventilatory failure, mouthpiece and lip-seal devices have also been used successfully. No comparison of success rates between nasal masks, full face masks, and other devices (eg, mouthpiece) has been reported. Mouthpieces and nasal masks facilitate communication and secretion clearance. Full face masks may offer more effective ventilatory support for acute respiratory failure, although there is no published experience with this in children (who are at increased risk for aspiration). For long-term use, patients may benefit from use of a variety of interfaces that can be alternated between daytime and nocturnal use and from day to day. For example, a simple mouthpiece may be kept adjacent to the mouth for easy accessibility during the day, with a lip seal added for nocturnal use; the addition of a bite plate may facilitate the use of an oral interface.

Table 4. Minimum Performance Characteristics for Ventilators Used for Noninvasive Positive Pressure Ventilation

	Type 1	Type 2
Ventilation Capabilities		
Mandatory rate	Yes, to 30 breaths/min	Optional
Assist capabilities	Yes	Yes
F_{IO_2}	0.21-0.5*	0.21 (optional up to 0.40)
Inspiratory pressures	to 30 cm H_2O†	to 30 cm H_2O†
PEEP	to 15 cm H_2O*	Optional, to 15 cm H_2O
2-hour battery backup	Optional	Optional
Pressure relief	Yes	Yes
Antiasphyxia capabilities	Yes	Yes
Airway attachments	Mask/mouthpiece	Mask/mouthpiece
Rebreathing potential‡	Minimal	Minimal
Inspiratory flow	60 L/min at 20 cm H_2O	60 L/min at 20 cm H_2O
ASTM circuit (resist/crimp)	Yes	Yes
Humidification	Optional	Optional
Leak tolerance	Yes	Yes
Monitors/Alarms		
Pressure monitor	Optional	Optional
Volume monitor	Optional	Optional
High pressure alarm	Optional	Optional
Disconnect alarm	Yes§	Optional
Power loss	Yes§	Optional
Battery loss	Yes (if battery present)	Yes (if battery present)

*In selected patients requiring long-term Type-1 support, PEEP and F_{IO_2} controls may not be necessary.
†Patients with severe skeletal deformities, severe restriction or obesity, or those subject to severe bronchospasm may require ventilators with higher pressure or volume capabilities.
‡CO_2 rebreathing should be measured by the manufacturer and reported in the operators' manual.
§Some chronic ventilator-dependent patients can sustain ventilation using glossopharyngeal breathings. In such patients, these alarms are optional.

B. Choice of Ventilator. The ventilator should be easily triggered to the inspiratory phase and easily cycled to the expiratory phase and should provide adequate flow to meet patient demand. For applications in acute respiratory failure, it is desirable to control the delivered oxygen fraction from 0.21 to 0.5. NPPV can be applied successfully using critical care ventilators, home care ventilators, or ventilators specifically designed for NPPV. Table 4 provides desirable characteristics.

C. Choice of Ventilator Mode. NPPV has been applied successfully using both volume and pressure ventilation. Pressure modes (pressure assist, pressure support, or pressure control) are preferred during acute respiratory failure because flow adjusts to meet the requirements of the patient. However, volume ventilation may be preferred by some patients with neuromuscular disease who sometimes need high tidal volumes for ventilation and coughing and for raising the volume of the voice during long-term use of NPPV.

D. Educational Aspects. The success of NPPV strongly depends on the skills of personnel caring for the patient. The goals and techniques (both cognitive and psychomotor) of applying NPPV must be thoroughly understood by the clinical team including respiratory therapists, nurses, and physicians. Training should include indications and complications of NPPV, coaching of patients to improve compliance, choice of appropriate interface, and choice of ventilator settings.

E. Application of NPPV. For initiation of NPPV:

- Choose a ventilator capable of meeting the patient's needs (usually pressure support ventilation or pressure assist/control but volume assist/control ventilation for selected patients).
- Choose the appropriate interface—face mask, nasal mask, mouthpiece, lip seal, or other device; take care not to use a mask that is too large—smaller is usually better.
- Explain the therapy to the patient and provide reassurance.
- Silence ventilator alarms and choose low settings (eg, inspiratory pressure of 5-10 cm H_2O and PEEP at lowest setting).
- Initiate NPPV while holding the mask (or other interface) in place; determine correct fit; choose alternate interface as necessary.
- Secure interface with head straps, avoiding an excessively tight fit (small leaks are acceptable). Mouth interfaces are secured with a bite plate.
- Titrate inspiratory pressure (or volume) to patient comfort (eg, reduced use of accessory muscles, respiratory rate, dyspnea).
- After assuring adequate ventilation, titrate oxygen con-

centration to maintain oxyhemoglobin saturation > 90% as indicated by pulse oximetry.
- Peak pressures > 25 cm H_2O are rarely needed with COPD; higher pressures may be safely used for other patient groups (eg, those with decreased chest-wall compliance).
- PEEP may be titrated to 5-10 cm H_2O to improve oxygenation or triggering (ie, to overcome auto-PEEP).
- Continue to coach and reassure the patient; make adjustments to improve patient acceptance: type and fit of interface, ventilator mode, inspiratory and expiratory pressure levels, volume versus pressure ventilation, F_{IO_2}, intermittent versus continuous use.

F. Weaning. For patients in acute respiratory failure, techniques for weaning from NPPV are unclear. Often, patients request time off NPPV. If the requested time off NPPV is well tolerated, then NPPV is often not restarted. However, NPPV should be re-established if the patient shows signs of respiratory distress when the mask is removed. The period of Type-1 NPPV for patients successfully treated is often short (< 2 days). Until the patient demonstrates a successful trial off NPPV with close monitoring for signs of respiratory distress, the mask should not be removed for diagnostic testing or routine nursing care. Such interruptions of NPPV may lead to decompensation and the need for emergency intubation.

V. Ethical Issues Related to Application of NPPV

In the setting of acute respiratory failure, the availability of NPPV has ethical implications regarding the interpretation of advance directives for "do not intubate." Because NPPV can provide life support without endotracheal intubation, health care providers must acquire a detailed understanding of what the patient means by "do not intubate." It is imperative to recognize the distinction between patients whose "do not intubate" directives indicate an absolute aversion to endotracheal intubation but a willingness to receive noninvasive ventilatory support (to whom NPPV should be offered) and those patients whose "do not intubate" directives reflect the desire to forego all acute resuscitative measures, even if noninvasively applied (in whom NPPV can be ethically deferred).

VI. Challenges to NPPV Research

Outcome research is needed to determine the cost-effectiveness of NPPV. In order to establish that NPPV is cost-effective, it must be shown that NPPV, compared to standard therapy, is:
- Better and less costly, or
- Equal and less costly, or
- Better and more expensive (but worth it).

Challenges in performing these studies include the need to identify appropriate patients (including children and those suffering from conditions other than COPD). Moreover, studies must demonstrate effectiveness (not just efficacy) using appropriate clinical (not just physiologic) relevant outcomes (eg, morbidity, mortality, length of stay, ventilator-free days.)

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Noninvasive Positive Pressure Ventilation: History and Terminology

David J Pierson MD

Introduction
History of Noninvasive Positive Pressure Ventilation
Use of NPPV in Resuscitation
Use of NPPV in Acute Respiratory Failure
Use of NPPV in Long-Term Care
Reasons for the Recent Increase in Interest in NPPV
Terminology & Classification of NPPV
Clarifying the Issues

Introduction

During the last decade, noninvasive positive pressure ventilation (NPPV) has become an accepted and widely used therapy for both chronic ventilatory insufficiency and acute ventilatory failure. The Consensus Conference that gave rise to this special issue of RESPIRATORY CARE was convened to clarify important clinical and technical issues relating to NPPV and to establish a context for the comprehensive reviews that comprise the bulk of the issue[1-9] and for the Consensus Statement developed by the Conference participants.[10] In this paper, I review the history of this form of assisted ventilation, point out some sources of confusion in terminology and other aspects of the literature on NPPV, and offer suggestions for reducing this confusion in the future.

History of Noninvasive Positive Pressure Ventilation

In theory, ventilation of the lungs can be supported in a variety of ways. Negative pressure can be generated around the lungs, expanding them passively as in normal spontaneous breathing. Gas can be forced into the lungs under positive pressure, either by an external source or by the patient's glossopharyngeal muscles; the elastic recoil of the lungs and thorax then return the lungs to functional residual capacity when the pressure is released. Alternatively, air can be squeezed out of the lungs by applying positive pressure to the outside of the chest wall, with functional residual capacity restored by the elastic recoil of the chest wall when the pressure is released. Or, the paralyzed diaphragm can be made to move alternately cephalad and caudad by repeatedly tipping the patient first head-down and then semi-upright, thus ventilating the lungs. Each of these strategies for artificial ventilation can be made to work, and has been applied clinically (Table 1). In addition, augmentation of gas exchange has been achieved without relying primarily on ventilating the lungs with gas, as shown in the last section of Table 1.

In the second half of the twentieth century, ventilatory support has been mainly via intermittent positive pressure ventilation (IPPV) through a cuffed endotracheal or tracheostomy tube. However, particularly since the mid-1980s, noninvasive ventilation has seen increasing application in both acute and long-term settings, for reasons discussed later. Negative pressure ventilation was widely used from the time of the great poliomyelitis epidemics of the first half of this century through the 1960s when better endotracheal tubes and positive pressure ventilators were made available.[11-14] Although several types of negative pressure ventilators remain available,[15-19] and their use in acute situations has seen some resurgence in recent years,[20] most noninvasive ventilatory support is now carried out via positive pressure and a variety of nasal, oral, or full-face interfaces, and it is on this manner of support that this review is focused.

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Table 1. Possible Ways To Support or Augment Ventilation and/or Gas Exchange

Move gas passively into lungs; exhalation passive
Spontaneous ('natural') breathing
External negative pressure to thorax (cuirass)
External negative pressure to whole body except for head (iron lung)
Move gas actively into lungs; exhalation passive
Intermittent positive pressure ventilation (breaths mandatory, assisted, supported, or spontaneous; machine- or patient-triggered; pressure-, volume- or flow-limited; machine- or patient-cycled)
Glossopharyngeal breathing (frog breathing)
Move gas actively out of lungs; inhalation passive
External positive pressure to abdomen and chest (pneumobelt)
Move gas passively into lungs; exhalation active
Alternating head-up and head-down positions, with diaphragm motion facilitated by shifting abdominal contents (rocking bed)
Other possibilities
Alternating compression/decompression of environment (barospirator)
Electrical stimulation of phrenic nerves to produce diaphragm contraction (electrophrenic respiration)
Gas exchange outside body via blood (extracorporeal membrane oxygenation; extracorporeal carbon dioxide removal)
Gas exchange inside body via blood (intravascular oxygenator)
Total or partial ventilation of the lungs with liquid (perfluorocarbon)

Use of NPPV in Resuscitation

The Bible contains at least two passages that bring NPPV to mind:

> And the Lord God formed man of the dust of the ground and breathed into his nostrils the breath of life. (Genesis 2:7)

> And he [Elisha] went up, and lay upon the child, and put his mouth upon his mouth and the flesh of the child waxed warm. (II Kings 4:34)

Although Vesalius, Harvey, and others had previously ventilated the lungs of cadavers and dogs by means of reeds inserted through the larynx and connected to a chimney bellows, successful resuscitation by means of mouth-to-mouth ventilation was first scientifically documented in the mid-1700s.[14,21,22] By the end of the eighteenth century, societies promoting the use of resuscitation had been formed both in the U.S. and in several European countries, primarily to increase survival after near-drowning. In 1780, Chaussier introduced the first bag-mask apparatus for NPPV as a substitute for mouth-to-mouth ventilation during resuscitation (Fig. 1).[22]

In the latter part of the nineteenth century, physiologists employed a variety of bellows-operated ventilators to ventilate animals during experiments, most commonly via a tracheostomy tube.[14,22] Dr George Fell, of Buffalo, was familiar with this use and adapted it for human application in 1887, using a face mask or nasal tube (Fig. 2).[22] It proved to be a substantial improvement over the various external artificial respiration methods then used worldwide for attempted resuscitation. Subsequently modified by O'Dwyer[23] and known as the Fell-O'Dwyer apparatus, this system became widely used in thoracic anesthesia, permitting continued ventilation while the chest was open.[22]

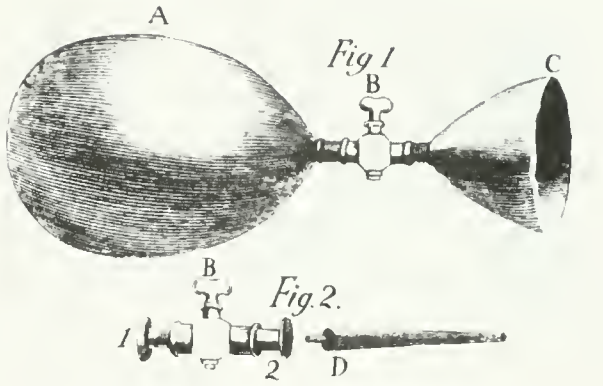

Fig. 1. Apparatus for manual positive pressure ventilation during resuscitation, as introduced by Chaussier in 1780. A bag made of leather or an animal bladder (A) was connected by means of a tap (B) to a leather mask (C). Alternatively, a metal tube (D) could be extended from the tap into the victim's nostril, permitting NPPV via the nasal route. (Reprinted from Reference 22, with permission.)

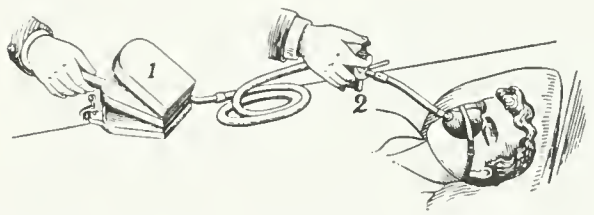

Fig. 2. The original Fell apparatus for artificial respiration during thoracic anesthesia, as introduced in 1887. A constant flow of air was produced by the bellows (1), and the anesthetist operated a "cornet valve" (2), either providing positive pressure during inspiration or venting it into the room. (Reprinted from Reference 22, with permission.)

Use of NPPV in Acute Respiratory Failure

Prior to the 1930s, developing acute respiratory failure meant certain death. There was no practical means for artificially ventilating the lungs outside the operating room. The forerunner of the modern iron lung had been devised by Drinker and Shaw in 1929,[11] and Emerson had shortly thereafter introduced a modified, more practical version,[24] but these did not see wide application until 1936. In that year, wide publici-

surrounded the successful use of a Drinker iron lung to support a patient with paralytic poliomyelitis during and after transport from China to the U.S.[24] The iron lung thus marked the beginning of clinically practical artificial ventilatory support (Table 2). During the next quarter century, many thousands of patients, most of them victims of polio, were successfully supported by means of tank ventilators, both during their initial acute illness and, in many cases, for years thereafter. The iron lung became a part of our culture: I remember visiting, in about 1960, a distant relative who had lived at home in one for nearly 20 years.

Table 2. Historical Factors in the Use of Noninvasive Ventilation To Treat Acute Respiratory Failure

1930s-1950s—Polio epidemics in U.S. and Europe; successful support if no underlying pulmonary disease
1960s—Widespread use of intermittent positive pressure breathing (IPPB), including application in acute exacerbations of chronic obstructive pulmonary disease (COPD)
1960s-1970s—Volume ventilators; improved endotracheal tube design; availability of arterial blood gas measurements; appearance of intensive care units
1970s-1980s—Increasing awareness of complications of invasive ventilation
1980s—Increasing experience with noninvasive ventilation in long-term settings other than postpolio; better masks; noninvasive ventilation used successfully in acute exacerbations of COPD
1990s—Increasing use world-wide; application in new clinical settings and diagnoses; first controlled trials

Prior to the introduction of a practical tank ventilator and before endotracheal intubation became widely available, a unique positive pressure device dubbed the barospirator was constructed in Sweden by Thunberg and subsequently tested by Enghoff.[13,14] The whole patient was enclosed in a rigid chamber, in which the pressure was alternately compressed and released. As long as the patient's glottis was open and lung volume stayed the same, the number of gas molecules in the lungs would increase when the chamber was compressed. An increase in ambient pressure of 55 torr resulted in an exhaled tidal volume of 500 or 600 mL when the pressure was released.[13,25] The barospirator could actually support gas exchange in the absence of spontaneous breathing, as documented in a series of 10 patients with paralysis following infection or drug intoxication, of whom 2 survived.[26]

A more practical approach to ventilatory support, one similar to the intermittent positive pressure ventilation in use today, was studied extensively by Motley, Werko, Cournand, and Richards at Bellevue Hospital in the mid 1940s.[23] These investigators had initially become interested in the application of expiratory positive airway pressure (EPAP) and continuous positive airway pressure (CPAP) via a rubber mask in high-altitude aviation. They utilized the same mask for IPPV, with and without EPAP, using first a pneumatic balance respirator (Burns model) and later a Bennett X-2 clinical research ventilator (Fig. 3),[23] in treating a variety of acute clinical conditions.

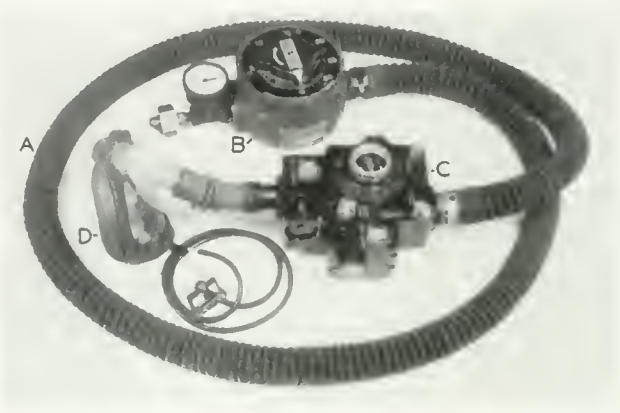

Fig. 3. The apparatus used by Motley and associates in the mid-1940s to deliver intermittent positive pressure ventilation, with or without positive end-expiratory pressure, to patients in acute respiratory failure. A corrugated rubber hose (A) connected a Bendix pressure demand regulator (B) to a Bennett Clinical Research Model X-2 respirator (C), from which air or oxygen was delivered to the patient by means of a Bennett face mask (D) (Reprinted from Reference 23, with permission.)

Motley and associates treated patients with acute pulmonary edema, pneumonia, Guillain-Barré syndrome, near-drowning, drug overdose, and acute asthma, using the apparatus shown in Figure 3.[23] They documented the deleterious effects of IPPV on cardiac output, and several of their recommendations astoundingly presaged current practice:

> The regulator should have a variable line pressure adjustment between 0 and 30 cm H_2O, and a high instantaneous flow rate without a significant drop in line pressure.[23]

In addition, Motley et al concluded that mask IPPV was most likely to succeed when the acute respiratory failure was of acute onset and short duration prior to therapy, when hemodynamic compromise was absent, and when pneumonia was absent. These statements coincide almost identically with the recommendations of this Consensus Conference 50 years later.[9]

IPPV by means of pressure-targeted ventilators and rubber face masks similar to those used by Motley was used throughout the 1950s and 1960s to treat patients with acute respiratory failure, particularly that complicating chronic obstructive pulmonary disease (COPD) and asthma. By the end of the 1960s, volume-targeted ventilators were available, arterial blood gases could be measured clinically, and intensive care units were being set up in many hospitals.

Periodic 10- to 20-minute IPPV treatments (intermittent positive pressure breathing, IPPB) had meanwhile become widespread in treating chronic lung disease and for delivering medications to the airways.[27] Although IPPB was often used in severe exacerbations of COPD or asthma, many clinicians frowned upon this, and IPPV via cuffed endotracheal or tracheostomy tubes became the standard of care. Despite documentation of a high incidence of complications related to intubation,[28,29] prevailing opinion held that ventilatory support without airway control was unacceptable because of the unpredictable tidal volumes and the risk of aspiration.

This began to change in 1989, when Meduri and colleagues reported successful management of 8 of 10 patients with acute respiratory failure (4/6 with COPD, 2 with congestive heart failure, and 2 with pneumonia) using pressure support ventilation via face mask (Fig. 4).[30] Other series quickly followed, illustrating that it was possible to ventilate patients noninvasively during acute respiratory failure of a variety of etiologies (Fig. 5).[31] The use of NPPV appeared especially attractive in treating acute exacerbations of COPD, and success was documented with both full face masks[32,33] and nasal masks,[34-37] using both pressure- and volume-targeted IPPV. Two groups of investigators reported the successful use of NPPV as a bridge to unassisted ventilation following intubation for acute respiratory failure.[38,39]

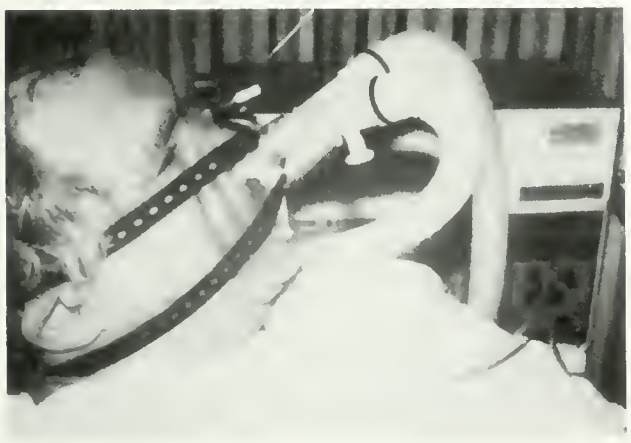

Fig. 4. Face mask ventilation as applied by Meduri and associates at the University of Tennessee in 1988. (Reprinted from Reference 30, with permission.)

Several authoritative reviews by experienced investigators in this field have concluded that NPPV is a useful and important addition to management.[40-45] As discussed by the participants of the Consensus Conference, knowledgeable caregivers and careful patient selection are of paramount importance, and controlled clinical trials are still needed to clarify several aspects of this therapy.[10]

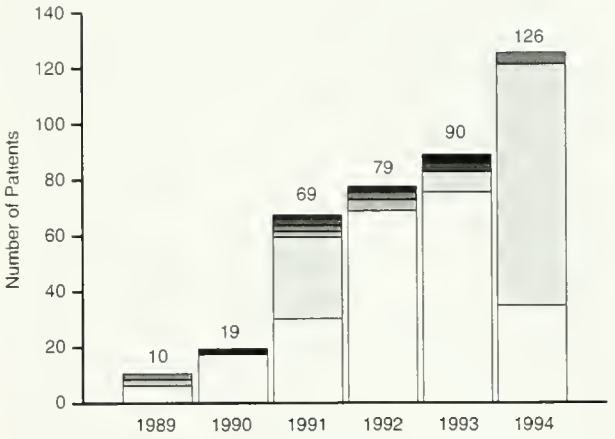

Fig. 5. Increasing published experience with noninvasive positive pressure ventilation in patients with acute respiratory failure, 1989-1994, as compiled by Sassoon. The majority consisted of patients with chronic obstructive pulmonary disease (COPD = □) and patients ventilated postoperatively (postop = □). Other includes restrictive thoracic disease (RTD = □), congestive heart failure (CHF = □), restrictive parenchymal lung disease (RPD = ■), and miscellaneous conditions (MISC = ■). Numbers above bars indicate total number of patients receiving NPPV in each year. (Reprinted from Reference 31, with permission.)

Use of NPPV in Long-Term Care

Providing ventilatory support for weeks, months, and even years to persons unable to breathe on their own became possible for the first time in the 1930s through the use of tank ventilators. Although the iron lung remained the primary means of support for the next 50 years, several adjunctive techniques were introduced along the way which enabled some patients to emerge from their tanks for at least part of the day.[13-15,24,46-48] The rocking bed, which shifts the abdominal contents cephalad and caudad by alternating between head-up and supine or slightly head-down positions, was introduced in 1932.[24] This was followed in 1938 by the first intermittent abdominal pressure ventilator, which forced air from functional residual capacity toward residual volume, followed by inspiration as the elastic recoil of the chest wall returned the lung to its previous volume.[49]

In New York in the late 1930s, Barach[25] modified the Thunberg barospirator, which Sahlin and others in Europe had used for managing acute respiratory failure.[26] Barach constructed separate chambers for the head and for the rest of the body in which the air could be compressed differentially. He called the device an equalizing alternating pressure chamber, and he attempted to rest the lungs of patients with tuberculosis through its use. Although he managed to ventilate 5 patients for an average of 12 hours/day for several months,[25] damage to their eardrums from the repeated pressure swings was a major problem, and the device saw little use thereafter.[12]

Although a device similar to the chest cuirass was described in 1904 for use in resuscitation,[50] the first mass-produced chest-shell ventilators were not introduced until 1949.[51] The Tunnicliffe breathing jacket, a wrap- or poncho-style negative-pressure ventilator, which operates much like the cuirass, followed in 1955.[52]

In about 1950, Dail and associates at the Rancho Los Amigos Respiratory Center for Poliomyelitis in Los Angeles observed that one of their patients, when out of his iron lung, breathed "in a peculiar manner, using his mouth and throat in what at first appeared to be a swallowing motion."[53] With the maneuver, this patient could breathe spontaneously for many hours; otherwise he could breathe unassisted for only a few minutes. Dail et al called this patient's spontaneously acquired ventilation technique glossopharyngeal breathing (GPB).[53] Other patients learned the technique spontaneously, and in 1955 Dail et al reported successfully instructing another 100 patients in its use.[53] One patient, whose spontaneous vital capacity was measured at 390 mL, was able to achieve an exhaled vital capacity of 2,250 mL using GPB.[53]

Glossopharyngeal breathing, also called gulping or frog breathing (because it is essentially identical to the manner in which frogs and other amphibians ventilate their lungs), has since been used by thousands of ventilator-dependent individuals as an auxiliary means of ventilatory support. It can be learned by noninvasively ventilated patients with little or no spontaneous vital capacity and can be effective both as an emergency measure in case of electrical power failure and as a means of being independent of mechanical support for periods of up to several hours.[54] In selected circumstances, it may also be possible to use GPB as a primary form of ventilatory support. Bach et al presented summary data on about 100 patients who were supported either totally or mainly by GPB, with or without the use of body ventilators.[55] This technique is also useful as an adjunct in coughing and secretion clearance.[24,56,57]

According to Bach,[56] NPPV via mouthpiece (Fig. 6) was first used at Goldwater Memorial Hospital in New York in the 1950s. Some patients who were totally ventilator-dependent and managed in tank ventilators were able to use NPPV by means of a mouthpiece during the daytime.[24] In 1993, Bach and associates reported on a 39-year experience with long-term ventilation, during which time 257 patients were successfully supported by mouth IPPV either alone or in combination with other techniques.[56]

Although success with long-term NPPV had been achieved at a few isolated centers of unique expertise for 25 years, widespread use of this form of support began only in the late 1980s (Table 3), in part as a result of developments in the treatment of obstructive sleep apnea (OSA). The first successful use of nocturnal CPAP via the nose in patients with OSA was reported by Sullivan and colleagues in Australia in 1981,[58] and was followed 2 years later by similar results in the obesity-hypoventilation syndrome.[59] Nasal CPAP rapidly became not only a widely used therapy but also a burgeoning industry, and a variety of pressure generators and patient interfaces were made available to clinicians. It was only a matter of time before these same interfaces were put to use in NPPV.

Fig. 6. Positive pressure ventilation via mouthpiece. This patient with Duchenne's muscular dystrophy had received 24-hour noninvasive ventilatory support for 14 years at the time of the photograph, via mouthpiece while awake and using a lipseal retention device during sleep. (Reprinted from Reference 56, with permission.)

Table 3. Historical Factors in the Long-Term Application of Noninvasive Ventilation

1930s—First practical tank ventilators: Drinker, 1929; Emerson, 1931
1940s—Negative pressure ventilation with tracheostomy for secretion management
1950s—Major polio epidemics: thousands of patients ventilated long term in Europe and U.S
1960s—Positive pressure ventilation via tracheostomy became standard of care. A few centers continued totally noninvasive ventilation using various combinations of tank ventilation, mouthpiece NPPV, intermittent abdominal pressure ventilation, and glossopharyngeal breathing. Widespread use of IPPB in patients' homes, especially in U.S.
1970s—Lightweight portable volume ventilators introduced; improved mouthpieces and lip-seal devices became available.
1980s—Nasal mask NPPV, initially with custom-made devices and then with commercial CPAP masks; successful patient experience reported from several countries
1990s—Proliferation of available interfaces, ventilators for NPPV, clinicians and users; application in increasing numbers of disorders and settings

In 1987, Sullivan's group reported the successful use of nocturnal NPPV via a nasal mask (Fig. 7) in managing chronic ventilatory insufficiency in 3 patients with postinfection muscle weakness and 2 with muscular dystrophy[60] and in a child

with nocturnal hypoventilation.[61] In that same year, Kerby et al[62] published their experience with this form of nocturnal ventilation in 3 patients with muscular dystrophy, 1 with amyotrophic lateral sclerosis, and 1 with central hypoventilation. Bach's group also reported successful nasal NPPV during 1987.[63]

Fig. 7. Apparatus for nocturnal nasal mask ventilation in patients with chronic ventilatory insufficiency, as reported in 1987 by Ellis et al. (Reprinted from Reference 60, with permission.)

The following year, Ellis et al[64] demonstrated successful use of nocturnal nasal NPPV in 7 patients with chest-wall deformity, and investigators in England reported its efficacy in 6 patients with chest-wall deformity and 4 with COPD.[65] Convincing evidence of the beneficial physiologic and clinical effects that could be achieved with nocturnal nasal NPPV was soon provided by Leger and associates in France, who documented marked improvement in chronic hypoxemia and hypercapnia during the daytime with long-term ventilation at night (Fig. 8).[66]

Since the appearance of these initial reports in the 'modern era' of long-term NPPV, there has been an explosion of interest in and experience with this therapy,[41,67-73] and several comprehensive reviews of its application are available.[5,42,49,74-76] There are now numerous choices of patient interface,[1,2,7,77,78] and both pressure and volume ventilators of manageable size and acceptable cost for home use.[78,79] Controlled trials have confirmed the value of long-term NPPV, at least in some patient populations.[10,36,80,81]

Reasons for the Recent Increase in Interest in NPPV

Interest in NPPV has increased dramatically in the last decade, and both interest and clinical experience continue to grow. Several factors have contributed to this growth (Table 4). As mentioned earlier, the recognition during the 1970s of

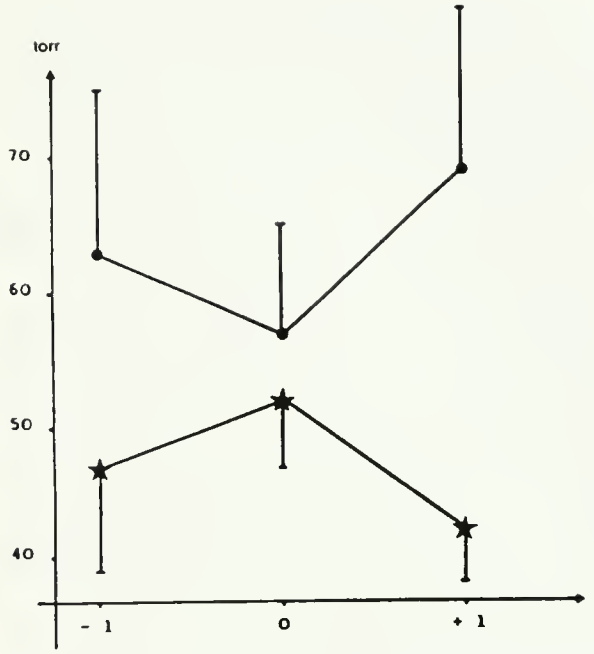

Fig. 8. Effect of nocturnal noninvasive positive pressure ventilation (NPPV) via nasal mask on arterial blood gas tensions in 17 patients with chronic ventilatory insufficiency, as reported in 1989 by Leger et al. P_{aO_2} = ●, P_{aCO_2} = ★. Point −1 on the horizontal axis represents data 1 year prior to the start of nocturnal ventilation; Point 0 indicates the deterioration that had occurred by the time NPPV was begun; Point +1 shows blood gas values obtained while the patients breathed room air spontaneously following 1 year of nocturnal NPPV. (Reprinted from Reference 66, with permission.)

obstructive sleep apnea and reports in the early 1980s of successful intervention using nocturnal nasal CPAP led to the introduction of effective nasal masks and set the stage for convenient, accessible NPPV. Introduction and subsequent international commercial availability of the portable BiPAP device (Respironics Inc), which could deliver both inspiratory pressure support and CPAP, enabled many clinicians to gain experience with NPPV as an elective therapy.

Table 4. Some Important Reasons for the Increased Interest in Noninvasive Positive Pressure Ventilation during the Last Decade (1986-1996)

- Success with nasal CPAP in obstructive sleep apnea
- Availability of better, more accessible patient interfaces
- Publication of reports of impressive successes in a few centers of expertise
- Increased appreciation of the role of the ventilatory muscles in both acute and chronic ventilatory failure
- Desire to avoid complications of intubation and tracheostomy
- Refusal of some patients to be intubated

At the same time, greater attention became focused on ventilatory muscle function as an important determinant of ver

tilatory insufficiency and acute ventilatory failure in patients with chronic neuromuscular and musculoskeletal disease. Reports from a few centers of unique expertise brought to wider attention the possibility of managing even totally ventilator-dependent individuals without tracheostomy.

In the intensive care unit (ICU), the desire to manage patients in acute respiratory failure without endotracheal intubation grew in part from a keener appreciation of the frequency and seriousness of complications related to artificial airways.[29,30] Particularly in the case of COPD, this led to attempts to rest the ventilatory muscles via NPPV through nasal or full face masks, and success in this patient population was followed by use of NPPV in other settings of acute respiratory failure.

Management of patients in acute respiratory failure without intubation could potentially decrease complications, reduce mortality, and shorten ICU and hospital stays. Absence of the tube could also diminish patient discomfort and make management easier for caregivers. The possibility of these benefits, most of them yet unproved, has nonetheless spurred wider application of NPPV in acute respiratory failure.

Another reason for today's increased interest in NPPV relates to the heightened awareness of patient preferences and focus on 'do not intubate' orders. Whether in refusing intubation patients are indicating a wish not to have any form of artificial support or desiring only to avoid the discomfort and loss of control associated with an endotracheal tube needs to be clarified. However, although these and other ethical implications of the use of NPPV in patients who refuse intubation remain unclear, this therapy is finding greater use in this setting.

Terminology & Classification of NPPV

Current interest and application of NPPV are the product of several distinct lineages. Intensivists have taken up NPPV as an alternative to IPPV via endotracheal tube in acutely ill patients, and they have generally used the ventilators, modes, and terminology of the ICU. For many of these ICU-based researchers, the context for NPPV has not extended beyond the acute-care setting. On the other hand, rehabilitation specialists and others caring for patients experiencing the post-poliomyelitis syndrome and others requiring total ventilatory support have looked to NPPV as a means for achieving greater independence and freedom from the disadvantages of both tracheostomy and the iron lung in their daily lives. And, clinicians caring long term for ambulatory patients with gradually progressive ventilatory insufficiency have approached NPPV as an elective, part-time therapy to rest the ventilatory muscles and slow the progression of disability. It should not be surprising that workers in these distinctly different clinical settings have described, approached, and thought about NPPV somewhat differently.

The schematic pressure and flow tracings shown in Figure 9 are those generated by the BiPAP ventilator, one of the most widely used devices for NPPV both in and out of the acute-care hospital. What should this output be called? Most clinicians call it BiPAP, but it has been my experience that the manufacturer insists that this copyrighted term be used only to describe its device and not a ventilation pattern or mode. What should the same pattern be called when it is generated by a different ventilator, of which several are now available for long-term use? I have heard it referred to as IPAP and EPAP (inspiratory and expiratory positive airway pressure, respectively); bilevel positive airway pressure; biphasic positive airway pressure; CPAP with inspiratory assist; and pressure support with PEEP. Hess and Kacmarek[82] have recently dubbed it "bilevel pressure assist." Consensus and standardization would help all clinicians interested in NPPV to communicate more clearly with one another.

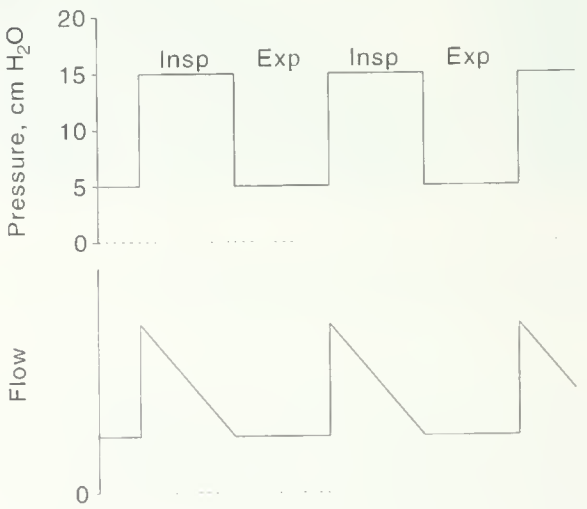

Fig. 9. Tracings of pressure and flow as might be detected at the mouth during two complete breaths with inspiratory positive airway pressure (IPAP) = 15 cm H_2O and expiratory positive airway pressure (EPAP) = 5 cm H_2O. Is this bilevel positive airway pressure, bilevel pressure-assist, or pressure support with PEEP? Or should it simply be called IPAP plus EPAP? Because the Respironics BiPAP ventilator produces a decelerating inspiratory flow and continuous expiratory flow, as shown in this example, and may be the most widely used home device that does so, should this pattern be referred to generically as BiPAP?

Ventilators and their functions should be referred to by the same terms and definitions regardless of their site and circumstances of use.[83] Fortunately, standardized terms and definitions are available. Developed with input from experts in all aspects of the design and technical application of positive pressure ventilators,[84-88] the American Association for Respiratory Care's Consensus Conference on the Essentials of Mechanical Ventilators[89] and its Consensus Statement[90] provide concepts and definitions that are applicable to devices used for NPPV. Wider adoption of the terminology and usage

in the Consensus Statement would greatly aid in clarifying communication about NPPV.

Clarifying the Issues

Not only with respect to terminology has the burgeoning literature on NPPV led to confusion, and although the latter has not been so profound as in the literature on weaning from ventilatory support,[91] the same potential exists for misinterpretation and misapplication. In this review, I have traced the history of NPPV separately for acute and long-term settings and have attempted to identify the diseases and clinical situations in which this therapy has been applied. The articles cited have amply shown that NPPV encounters different problems and has varying degrees of success in different patient populations and clinical settings. Reports of research on NPPV and guidelines for its application should specify the disease, the acuteness of the patient's condition, and the location in which NPPV is used (Table 5). Likewise, details of the ventilation approach and technique should be provided, as should the type of mask or other patient interface used. The Consensus Statement that accompanies this article[10] goes a long way toward this goal of standardization and serves as an example of the precise and rational use of terminology and techniques relating to NPPV.

Table 5. Suggestions for Clarity and Avoidance of Confusion in Communication about Noninvasive Positive Pressure Ventilation

- Identify the patient and clinical setting
  - What disease?
    - Obstructive vs restrictive vs neuromuscular vs other
    - Hypoxemia vs hypercapnia
    - Parenchymal lung disease vs impaired chest bellows function vs central drive problem
  - What circumstances?
    - Acute respiratory failure vs chronic insufficiency
  - What location?
    - Emergency room vs intensive care unit vs ward vs home
- Describe the ventilation approach and technique
  - Continuous or intermittent? (life support vs elective or semi-elective therapy)
  - Positive pressure on inspiration, expiration, or both?
  - Pressure- or volume-targeted?
- Specify the ventilator-patient interface
  - Nasal mask vs face mask vs mouthpiece vs intra-oral appliance

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Characteristics of Pressure-Targeted Ventilators Used for Noninvasive Positive Pressure Ventilation

Robert M Kacmarek PhD RRT

Introduction
General Description
Modes of Ventilation
Comparison of Characteristics
- **Ability To Meet Peak Inspiratory Demand**
- **Inspiratory Sensitivity**
- **Expiratory Sensitivity**
- **Rise Time**
- **CO_2 Rebreathing**

Portable Pressure-Targeted Ventilators
- **Limitations**
- **The Ideal Portable PTV**

Introduction

Noninvasive positive pressure ventilation (NPPV) is not a new concept. Patients have been receiving ventilatory assistance noninvasively by mask since the late 1950s,[1] and reports of patients supported noninvasively by mask appear in the literature as early as the 1970s.[2] However, the use of NPPV in the intensive care unit (ICU) fell into disfavor in the late 1970s because of the poor outcomes associated with the noninvasive use of intermittent positive pressure (IPPB) devices on a continuous basis, the refinement of volume ventilators and the emphasis on the use of volume ventilation in the ICU, and the anti-IPPB attitude of the 1970s and 1980s.[3,4]

As discussed in other papers appearing in this issue of RESPIRATORY CARE,[5-12] our knowledge of how to apply NPPV has grown tremendously as have the data supporting its use in acute respiratory failure.[13-18] In particular, based on the abundance of data from prospective randomized clinical trials,[15-18] the use of NPPV should be the standard of care in COPD patients presenting in an acute exacerbation and this therapy should be available to all COPD patients presenting in acute distress, regardless of institution.

My objective in this paper is to discuss the functional characteristics of the class of portable pressure-targeted ventilators (PTVs) that have been designed exclusively for use with patients requiring NPPV. In addition, I discuss the limitations of these ventilators and define what I consider to be the optimal portable PTV for use in NPPV.

General Description

The ventilators classified as portable PTV include BiPAP devices* and are known as bi-level CPAP ventilators or bi-level-pressure ventilators.[20-24] All of these ventilators are compressor/blower driven and electrically powered, and almost all of the currently available models are unable to accept a high pressure (50 psi) gas source.[25] As a result, delivery of high (> 40%) or precise oxygen concentrations is impossible. In general, these devices can be considered continuous

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*Suppliers of commercial products are listed in the Product Sources section at the end of the text.

flow ventilators in which flow delivery is based on the set positive end-expiratory pressure (PEEP), set inspiratory pressure level, and patient demand. Most use a single-circuit gas delivery system without a true isolation exhalation valve. This can lead to rebreathing of exhaled gas as I discuss later.[22,23,26]

Modes of Ventilation

Some manufacturers have used IPAP (inspiratory positive airway pressure) and EPAP (expiratory positive airway pressure) to define the approach used to deliver gas (Fig. 1) with these ventilators. However, all of the models currently available (1997) deliver either pressure support or pressure assist/control, with or without PEEP. Many also can provide CPAP without ventilatory support. During CPAP, a few devices have time-delay options or CPAP 'ramping' options (slow rise in CPAP level before reaching set target). Assist (ie, pressure support), assist/control, and control ventilation are available on various current devices (Table 1). In addition, some devices allow adjustment of the inspiratory and expiratory sensitivities. Others allow a variation in the time required for inspiratory pressure to achieve the set peak-airway pressure (ie, the rise time). The inspiratory sensitivity mechanism in most devices is flow based. The few models with expiratory sensitivity allow a variation in end-inspiratory flow that results in cycling to expiration. In a few models, inspiratory time can be set in the control mode.

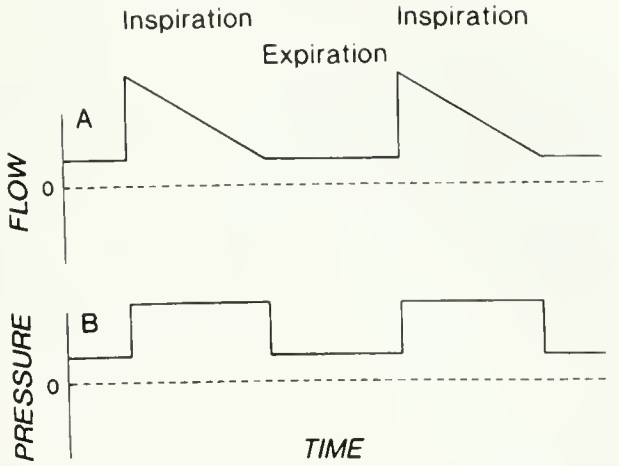

Fig. 1. A. Continuous expiratory flow and decelerating inspiratory flow characteristic of portable pressure-targeted ventilators (PTVs). The level of end-inspiratory flow depends on the mode of ventilation, total system peak pressure, and patient ventilatory pattern. B. Inspiratory pressure plateau and expiratory PEEP established with portable PTVs.

Comparison of Characteristics

Ability To Meet Peak Inspiratory Demand

As a group, the portable PTVs are capable of providing variable and high initial peak flows.[20-24] Strumpf et al,[20] on a lung model and in 4 patients who had been receiving nocturnal ventilatory assistance with volume-targeted, portable ventilators or nasal CPAP, showed that the BiPAP ventilator was able to deliver high peak inspiratory flow (Fig. 2). Flow peaked rapidly at the onset of inspiration but also rapidly decelerated to a lower end-inspiratory level, dependent upon compliance and resistance of the system. As with all pressure-targeted modes of ventilation, tidal volume (V_T) increased as inspiratory pressure target and inspiratory time increased (Fig. 3[20]). Extending inspiratory time to a level that resulted in air trapping decreased volume delivery. They also showed that in 2 of the patients ventilated, long-term, nocturnal use of the device reduced P_{aCO_2} by 15 and 20 torr.[21]

Lofaso et al[22] in a 1995 publication compared the BiPAP ventilator with its normal orificial exhalation port to the BiPAP ventilator with a nonrebreathing isolation valve on a lung model and in a series of patients who were being maintained in the pressure support mode on a variety of ICU ventilators. They noted that the use of an isolation nonrebreathing valve to pre-

Table 1. Operational Characteristics of Representative Portable Pressure-Targeted Ventilators

Ventilator*	Modes	Adjustable Controls?				
		Inspiratory Sensitivity	Expiratory Sensitivity	Rise Time	Inspiratory Time	Maximum Inspiratory Pressure (cm H_2O)
STD-20	Assist, assist/control, control, CPAP	No	No	No	Up to 90%	20
STD-30	Assist, assist/control, control, CPAP	No	No	No	Up to 90%	30
320 I/E	Assist, CPAP	Yes	Yes	No	No	20
PB 335	Assist, assist/control, control, CPAP	Yes	Yes	No	No	20
O'NYX	Assist, assist/control	Yes	Yes	No	Up to 80%	40
Ventil+	Assist, assist/control/control, CPAP	No	No	No	Up to 55%	30
VPAP	Assist, CPAP	No	No	No	No	20
Quantum	Assist, assist/control, control, CPAP	Yes	No	Yes	No	20
DP-90	Assist, CPAP	No	No	No	No	No

*Suppliers identified in Product Sources section at end of text.

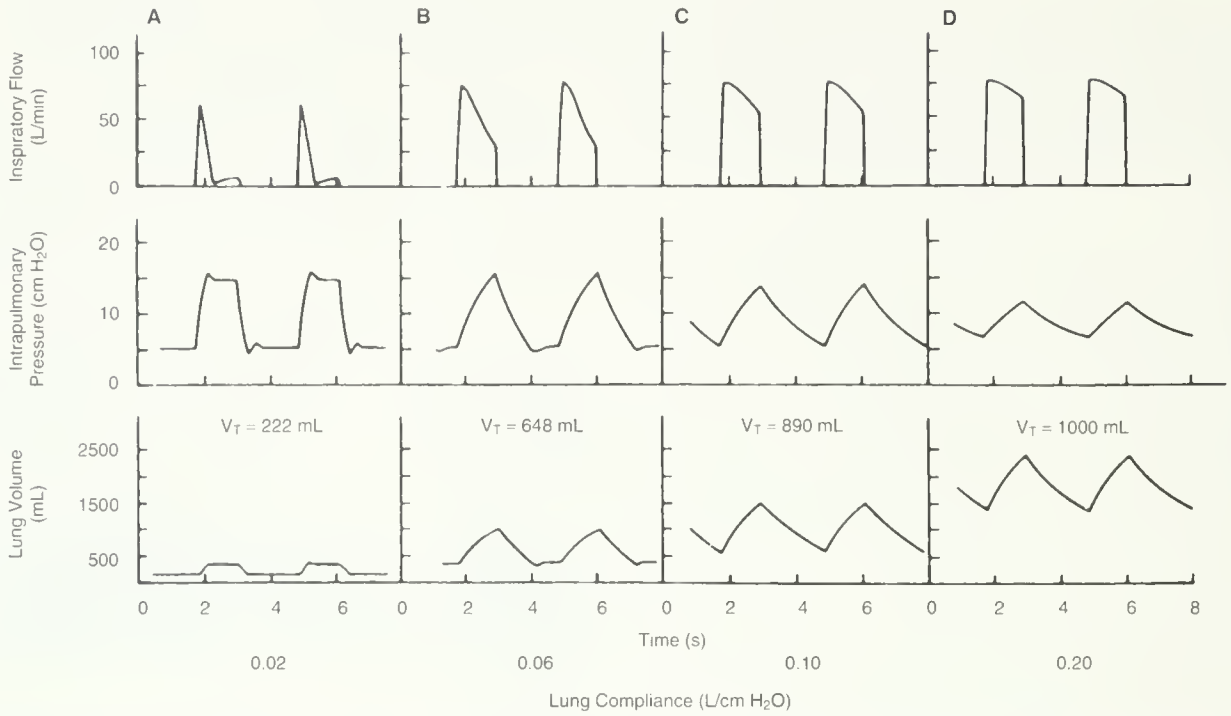

Fig. 2. Simultaneous inspiratory flow, intrapulmonary pressure, and lung volume across a range of compliances in a lung model. Rate is 20/min; PEEP 5 cm H_2O; % inspiratory time 40%; and airway resistance 4.6 cm H_2O s $\cdot$ L^{-1}. (Reprinted from Reference 19, with permission.)[20]

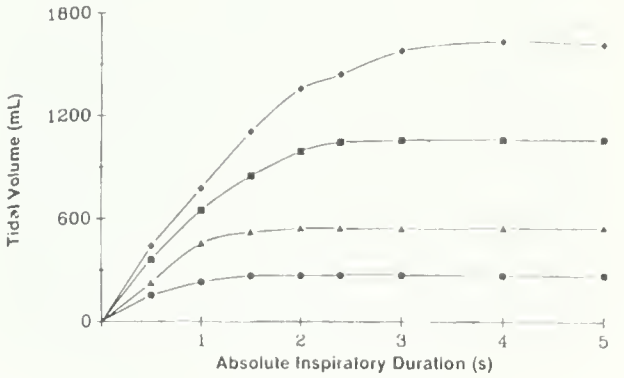

Fig. 3. Tidal volumes from a lung model at inspiratory times of increasing length at various pressure control levels. ◆ = 15 cm H_2O, ■ = 10 cm H_2O, ▲ = 5 cm H_2O, ● = 2 cm H_2O. PEEP is 5 cm H_2O, lung compliance 0.1 L/cm H_2O and airway resistance 4.6 cm H_2O s L^{-1}. (Reprinted from Reference 20, with permission.)

vent the rebreathing of CO_2 decreased the speed with which peak flow was achieved in their lung model (Fig. 4) and increased PEEP, resulting in a decreased V_T. In patients, BiPAP with the nonrebreathing isolation valve resulted in work-of-breathing (WOB) and blood-gas values equivalent to those observed with the ICU volume ventilators that maintained these patients. However, use of the BiPAP ventilator with its standard orificial exhalation port also maintained the same arterial blood gas values but resulted in a 50% increase in the WOB and increases in minute ventilation and breathing frequency. In all comparisons, PEEP was set at zero or minimum on each ventilator. The greater WOB with the standard BiPAP setup was attributed to the rebreathing of CO_2.

In a subsequent comparison, Lofaso et al[23] compared a series of portable PTVs to an ICU pressure support ventilator, the ARM-25, using a lung model. Of the 6 portable PTV systems evaluated, 3 were capable of matching the peak flow of the ARM-25 ventilator. However, the ARM-25 ventilator's ability to accelerate flow exceeded that of all other devices tested (Table 2), but the work performed on the lung model by most of the ventilators evaluated was similar to that performed by the ARM-25.

Our group, led by Bunburaphong,[24] recently compared 9 portable PTV to the Nellcor Puritan Bennett 7200ae adult critical care ventilator using a lung model. We found that the peak flow delivered by all portable PTV equaled or exceeded that of the 7200ae (Table 3) and that all but 2 of the 9 portable PTV achieved a more ideal airway-pressure profile during inspiration than did the 7200ae. The actual inspiratory airway-pressure profile, as shown in Figure 5, was compared to a perfect rectangle beginning at the onset of inspiratory effort with pressure instantaneously achieving the target set. Profiles achieved with each ventilator were expressed as a percentage of the area of the ideal profile (Area I %).

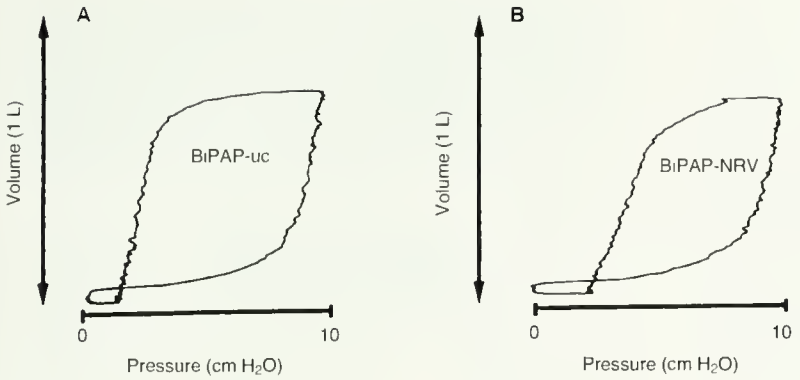

Fig. 4. Pressure-volume curves from the BiPAP A. with whisper swivel (BIPAP-uc) and B. with nonrebreathing valve (BiPAP-NRV) during a lung model 'breath.' PEEP was higher and inspiratory flow took longer to peak with the BIPAP-NRV. Consequently, tidal volume was slightly lower with the BIPAP-NRV than with the BIPAP-uc. (Reprinted from Reference 22, with permission.)

Table 2. Performance Characteristics of Representative Portable Pressure-Targeted Ventilators*

Variable	ARM25†	O'NYX	Vential	BiPAP-NVR	BiPAP-WS	Ventil+	Companion 320
% work performed by ventilator during inspiration	87.2 (1.7)	81.5 (1.5)‡	89.9 (3.1)	82.7 (1.1)‡	79.6 (1.0)‡	82.4 (1.2)‡	86.5 (1.7)
Flow acceleration up to 85% of peak ($L \cdot s \cdot s^{-1}$)	13.5 (0.5)	12.7 (0.3)‡	5.0 (0.7)‡	6.8 (0.3)‡	6.5 (0.9)‡	3.9 (0.2)‡	11.8 (1.2)‡
Pressure-time product (cm H_2O s)§	0.050 (0.0004)	0.046 (0.008)	0.137 (0.017)‡	0.163 (0.008)‡	0.076 (0.003)‡	0.129 (0.009)‡	0.070 (0.008)‡
Expiratory work imposed on lung model (J/L)	0.08 (0.00)	0.16 (0.00)‡	0.05 (0.00)‡	0.21 (0.00)‡	0.12 (0.00)‡	0.04 (0.00)‡	0.10 (0.00)‡

*Modified from Reference 23.
† All values are mean (SD). Inspiratory pressure set at 10 cm H_2O, expiratory pressure at minimum.
‡ $p < 0.05$ compared to ARM 25.
§ At beginning of inspiration when airway pressure is below PEEP.

Table 3. Inspiratory and Expiratory Trigger Capabilities and Peak Flows of Portable Pressure-Targeted Ventilators*

	Ventilator Assessed									
Assessed Variable	STD-20	STD-30	320 I/E	335	O'NYX	VPAP	Ventil+	Quantum	DP-90	7200ae
D-I (ms)	97 (15)†	93 (10)†	90 (10)†	108 (11)†	107 (106)†	271 (61)†	180 (13)	180 (45)	146 (47)	162 (81)
P-I (cm H_2O)	1.6 (0.6)†	1.4 (0.5)†	1.1 (0.4)†	1.6 (0.6)†	1.7 (0.7)†	1.5 (0.7)†	2.5 (0.7)†	2.1 (0.9)†	1.3 (0.5)†	3.6 (1.8)
D-E (ms)	104 (99)	77 (8)†	69 (9)†	9 (107)†	25 (191)†	449 (251)†	91 (62)	22(109)†	332 (263)†	174 (93)
P-E (cm H_2O)	3.3 (1.4)†	2.8 (1.1)†	2.3 (0.9)†	3.1 (1.5)†	5.5 (2.3)	3.7 (1.5)†	4.0 (1.5)†	4.6 (2.0)	4.0 (1.8)	5.3 (2.3)
Area-I %	73 (5)†	83 (1)†	82 (2)†	75 (4)†	65 (18)†	41 (9)†	64 (4)†	51 (9)	62 (10)†	55 (15)
Peak Flow (L/min)	76 (21)†	82 (23)†	80 (21)†	79 (23)†	68 (18)	60 (17)	89 (19)†	63 (20)	67 (17)	65 (18)

*Modified from Reference 24. Suppliers identified in Product Sources section at end of text.
D-I = time between initiation of inspiratory effort and the increase in pressure above baseline; P-I = decrease in pressure from baseline (ie, below baseline) during the triggering phase; D-E = time delay from the onset of expiration until airway pressure falls below baseline; P-E = increase in pressure above set pressure level at end inspiration; Area-I% = actual compared to ideal area of inspiratory pressure curve.
† $P < 0.05$ vs 7200ae.

In general, once triggered, most currently available portable PTV either equal or exceed the flow delivery capabilities of ICU ventilators. As was first discussed by Marini et al in 1986,[27] initial peak flow capabilities determine the ability of ventilators to meet the ventilatory demand of patients. Over all, pressure-targeted modes of ventilation are better suited to meeting patient demand than are volume-targeted modes because of their ability to vary flow delivery based on inspiratory pressure settings and patient demand.[28] It seems clear, based on the currently available literature, that portable PTVs compare well with standard ICU ventilators in meeting the ventilation demands of patients.[20-24]

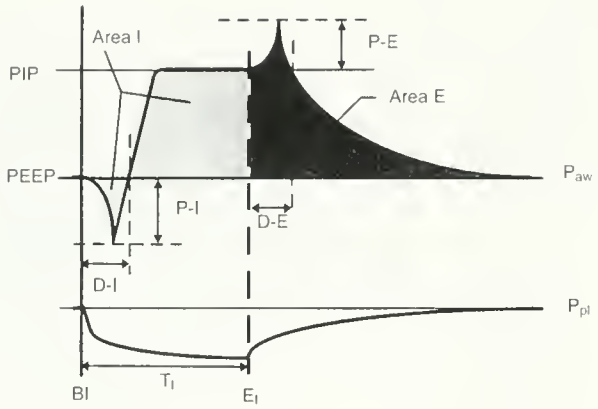

Fig. 5 The variables used to evaluate the function of 9 portable pressure-targeted ventilators and the 7200ae ventilator: BI, beginning of inspiration; EI, end of inspiration; T_I, inspiratory time; D-I, inspiratory delay time; P-I, inspiratory trigger pressure; Area I, inspiratory area; D-E, expiratory delay time; P-E, supraplateau expiratory pressure change; Area E, expiratory area; PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; Ppl, simulated pleural pressure; P_{aw}, airway opening pressure. (Reprinted from Reference 24, with permission.)

Inspiratory Sensitivity

A number of studies[29-31] have addressed the triggering of ventilator demand-CPAP systems and have shown clearly that flow-triggered systems outperform pressure-triggered systems. However, our group (Goulet et al[32] has shown in 10 patients that with the 7200ae ventilator in the pressure support mode (using a pressure trigger), inspiratory sensitivity set at −0.5 cm H_2O performed better than flow-triggering set at 2 L/min (5 L/min base flow). All of the currently available PTVs use a flow-triggered inspiratory sensitivity, and most are factory set and are not adjustable.

When one compares the responsiveness of ventilators, two primary features of the ventilator response should be assessed: time delay and system pressure change or inspiratory trigger pressure. The time delay (D-I) is generally defined as the time between initiation of inspiratory effort and the increase in pressure above baseline (Fig. 5); whereas, pressure change (P-I) is the decrease in pressure from baseline (ie, below baseline) during the triggering phase of assisted ventilation. D-I ideally should be a few milliseconds at the P-I equal to the sensitivity setting. However, because of delay in recognition of patient effort by the ventilator, delay in activating gas delivery mechanisms, and resistance to flow, both the D-I and P-I with many ventilators is excessive.[25]

Lofaso et al[22] reported from a lung model evaluation that the pressure necessary to trigger the BiPAP device with its normal orificial exhalation port was −1.4 (0.1) cm H_2O (mean, SD) and −2.6 (0.2) cm H_2O when a nonbreathing, isolation exhalation valve was used. In a later study of 5 portable PTVs and the ARM 25, Lofaso et al[23] reported the inspiratory trigger pressure-time product based on the P-I and D-I during triggering in a lung model evaluation. They found that the Pierre Medical O'NYX was the only device that performed as well as the ARM 25 and that for some ventilators the pressure-time product was up to 300% greater than in the ARM 25 (Table 2).

Our recent study[24] of 9 portable PTVs compared to the 7200ae, the STD30, 320 I/E, O'NYX, 335, and the STD 20 demonstrated a shorter D-I than the 7200ae. The P-I observed with the STD 30, VPAP, 320 I/E, O'NYX, Ventil+, 335, STD20, Quantum, and the DP90 was less than the P-I with the 7200ae.

When results are reviewed, especially when the data in Table 2 and 3 are compared, it seems reasonable to state that portable PTVs with preset or adjustable inspiratory triggers perform as well as ICU ventilators, with many exceeding the inspiratory trigger performance of some ICU ventilators. As with all ventilators in which the sensitivity can be set, the portable PTV should be set at the most sensitive setting that does not result in auto-cycling.

Expiratory Sensitivity

The PSV mode on ICU ventilators triggers to exhalation when a preset end-inspiratory flow is achieved or the end-inspiratory flow equals a preset percentage of the peak inspiratory flow. The same is true for portable PTV—a specific end-inspiratory flow threshold must be met before cycling occurs. Although at first this may seem ideal, MacIntyre et al[33] (Fig. 6) and more recently Jubran et al[34] have suggested that a fixed end-inspiratory flow trigger may result in activation of expiratory accessory muscles of ventilation, the imposition of expiratory WOB, and increased ventilatory drive. Whenever the end-inspiratory pressure increases above the inspiratory pressure target level (Fig. 6) just prior to exhalation, abdominal muscle activation has occurred to force cycling to exhalation. Many ventilators utilize a pressure increase above set peak pressure as a secondary cycling mechanism to exhalation. Jubran et al[34] have noted that secondary pressure cycling to exhalation in pressure support is common in patients with COPD, as a result of increased recoil of the lung and thorax because of expiratory muscle activation. This phenomenon is most common in patients with COPD because COPD patients have inspiratory flow patterns that differ from those in patients without obstructive lung disease. In COPD, the initial peak inspiratory flow tends to be low because of mechanical limitation or weakness unless ventilatory drive is markedly increased, and the normal deceleration to a near-zero end-inspiratory flow before beginning exhalation is usually absent in these patients, especially those in acute failure. Instead, COPD patients tend to begin exhalation when end-inspiratory flows are high, preventing appropriate triggering to the expiratory phase. This situation can be identified easily in many COPD

patients maintained on pressure support by looking for an end-inspiratory increase in system pressure (Fig. 6). If the airway pressure exceeds target setting at the onset of exhalation, activation of expiratory muscles has occurred to trigger to the expiratory phase.

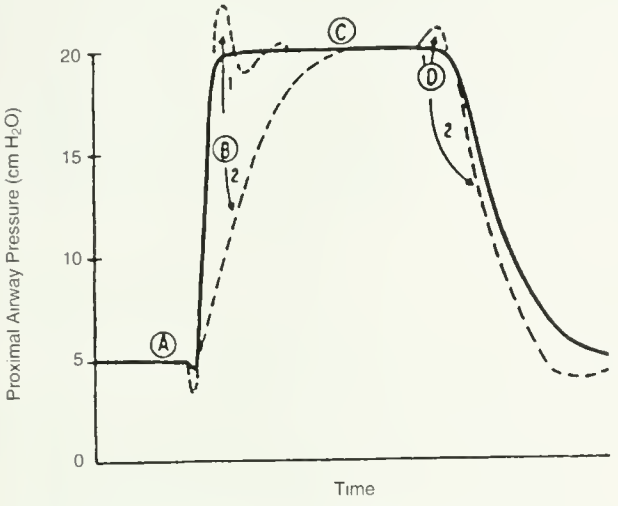

Fig. 6. Design characteristics of a pressure-supported breath. In this example, baseline pressure (PEEP) is set at 5 cm H_2O and pressure support is set at 15 cm H_2O (PIP 20 cm H_2O). The inspiratory pressure is triggered at Point A by patient effort, resulting in a decrease in airway pressure. Demand valve sensitivity and responsiveness are characterized by the depth and duration of this negative pressure. The rise to pressure (Line B) is provided by a fixed high initial flow delivery into the airway. Note that if flow exceeds patient demand, initial pressure exceeds set level (B1), whereas if flow is less than patient demand, a slow ('concave') rise to pressure occurs (B2). Plateau of the pressure support (Line C) is maintained by servo control of flow. A smooth plateau reflects appropriate responsiveness to patient demand; fluctuations reflect less responsiveness. Termination of pressure support occurs at Point D and should coincide with the end of spontaneous inspiratory effort. If termination is delayed, the patient actively exhales (bump in pressure above plateau) (D1); if termination is premature, the patient continues expiratory activity (D2). (Reprinted from Reference 33, with permission.)

In our recent study,[24] we compared the pressure change on expiration (P-E) and the time delay for exhalation, D-E, (from the onset of expiration until airway pressure fell below baseline) in a lung model for 9 portable PTVs and the 7200ae ventilator. We observed P-Es expressed as mean (SD), ranging from 2.3 (0.9) to 5.3 (2.3) cm H_2O and D-Es from 9 (107) to 449 (251) ms (Table 3). Again the portable PTVs generally performed as well as or better than the 7200ae, but over all most performed poorly in this regard. The reasons for the high P-Es and long D-Es were a combination of the lack of coordination between the lung model's 'deciding' to passively exhale, the ventilator's end-inspiratory flow-expiration triggering criteria, and resistance to expiratory flow imposed by the ventilator circuit. Because most of these ventilators use an exhalation port with a small orifice and maintain PEEP by continuous flow, expiratory resistance is high. In fact, Lofaso et al[13] observed between 0.04 (0.00) and 0.21 (0.00) J/L of imposed expiratory work both in lung models and in patients using these ventilators. Further, we noted[24] that the expiratory area (Area E, as seen in Figure 5) was markedly increased with most ventilators evaluated.

Both the Nellcor Puritan Bennett 335 and 320 I/E and the O'NYX incorporate adjustable end-inspiratory triggers. This control should assist in ensuring a better match between the ventilator's initiation of exhalation and the patient's desire to begin the expiratory phase. Figure 7 illustrates unpublished data from the study by our group[24] regarding the end-inspiratory trigger in the 335. At the Number 1 setting of the trigger, lung model exhalation preceded the ventilator's transition to the expiratory phase. This resulted in a marked decrease in simulated intrathoracic pressure at the end of inspiration. At the Number 2 setting, the ventilator only slightly preceded the lung model cycling to exhalation, while, at the Number 5 setting, the lung model preceded the ventilator in cycling to exhalation, resulting in a spike in the airway pressure at the end of the inspiratory phase. As shown in Figure 7, it is difficult to set the end- expiratory trigger even when waveforms of airway pressure and flow are available. Without waveforms, which are not available on either the 335, the 320

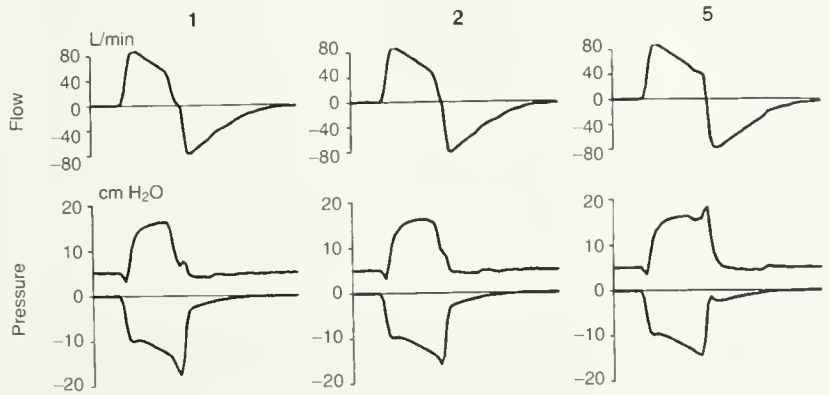

Fig. 7. Flow, airway pressure (+ deflection), and simulated intrathoracic pressure (– deflection) in a lung model at various expiratory trigger settings on the Nellcor Puritan Bennett 335 Ventilator. At Setting 1, the ventilator cycled to exhalation before the lung model, resulting in a spike in the intrathoracic pressure. At Setting 2, the ventilator and lung model are almost in synchrony while cycling to expiration. At Setting 5, the ventilator is cycling to expiration after the lung model has begun expiration.

I/E, or the O'NYX, or an airway manometer or pressure indicator, it may be impossible to properly set this control (the O'NYX has a digital airway pressure indicator). Clinical assessment for recruitment of accessory muscles of expiration and ventilatory drive may be the only methods of determining the proper setting of this control.

Rise Time

As discussed earlier, the speed with which the targeted inspiratory pressure is met can be varied. Some ICU ventilators include this option and one portable PTV, the Quantum, also includes this control. However, neither patient nor lung model data on its operation are available. This can be a useful control because many patients like a rapid rise in airway pressure to the targeted level, while others prefer a more gradual increase. As illustrated in Figure 6, a rapid rise in system pressure can cause the initial rise to overshoot the set pressure. Of concern with the Quantum is the lack of an airway pressure or flow waveform. Without visual indicators of pressure and flow, it is difficult to select the appropriate setting for the rise time. The Quantum does have a digital pressure indicator, which is helpful in setting this control.

CO_2 Rebreathing

A unique problem with all portable PTVs that do not incorporate an isolation-type exhalation valve is the rebreathing of exhaled CO_2.[22,23,26] This occurs primarily when PEEP is set at minimum. With these ventilators, exhalation usually occurs via a small orifice at the distal end of the inspiratory tubing, and when PEEP is set at zero or minimum, little flow moves through the circuit during expiration. As a result, the route of least resistance is retrograde movement of exhaled gas into the delivery tubing. As indicated in Figure 8,[26] this may result in the rebreathing of as much as 20 mL of CO_2/breath in volunteers and 12 mL of CO_2/breath in patients. The problem as shown in Figure 8 can be almost totally eliminated if an isolation-type exhalation valve is added to the circuit or if PEEP is set > 4 cm H_2O. When Ferguson and Gilmartin[26] compared the effects of the BiPAP ventilator with a whisper-swivel exhalation valve to a typical volume-cycled home care ventilator and the BiPAP ventilator with an isolation-type exhalation valve in a series of patients with CO_2 retention (Fig. 9), the BiPAP ventilator with the whisper-swivel exhalation device failed to lower the patient's P_{aCO_2}. This potential for CO_2 rebreathing is of marked concern if a face mask is used to ventilate a patient in an acute exacerbation of COPD. The large mechanical dead space of some masks coupled with the potential for rebreathing because of the exhalation mechanism design may result in the failure of NPPV. With a nasal mask, most patients partially exhale through their mouth, minimizing the potential for CO_2 rebreathing. This alternative is unavailable if a full face mask is used.

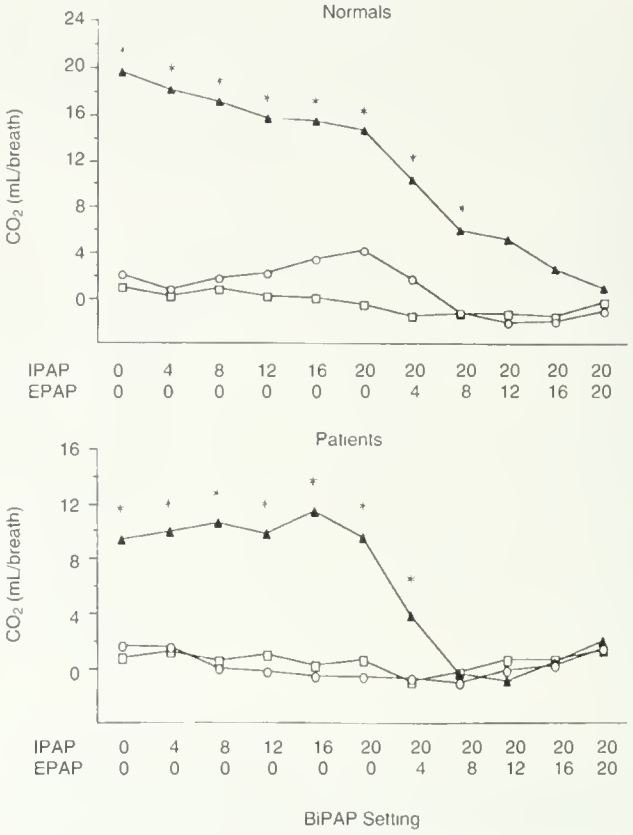

Fig. 8. Volume of CO_2 inhaled from the ventilator tubing at various IPAP and EPAP settings during BiPAP ventilatory assistance in normal subjects (top) and patients (bottom). Whisper-Swivel = ▲, Plateau = ○, Nonrebreather = □. *Indicates $p < 0.05$ compared with other devices at similar BiPAP settings. (Reprinted from Reference 26, with permission.)

Portable Pressure-Targeted Ventilators

Limitations of Portable PTV

In addition to the potential for rebreathing of CO_2, the portable PTVs are unable to deliver precise, consistent, and high oxygen concentrations, and most of these ventilators have no alarms or monitors. The exception is the Quantum, which does display airway pressure change and includes alarms for pressure, disconnection, and ventilator malfunction. These three major limitations in the capabilities of these ventilators cause me to strongly recommend against their use in the ICU for the management of acute respiratory failure, regardless of the cause. Based on current design, I believe that these devices should be used only on patients who require only periodic NPPV and should never be attached to an artificial airway. The reason for this strong statement is patient safety. Without correction of these major deficiencies in the operation of the portable PTVs, I believe that they are unsafe for use with patients requiring continuous ventilatory support—acute or chronic.

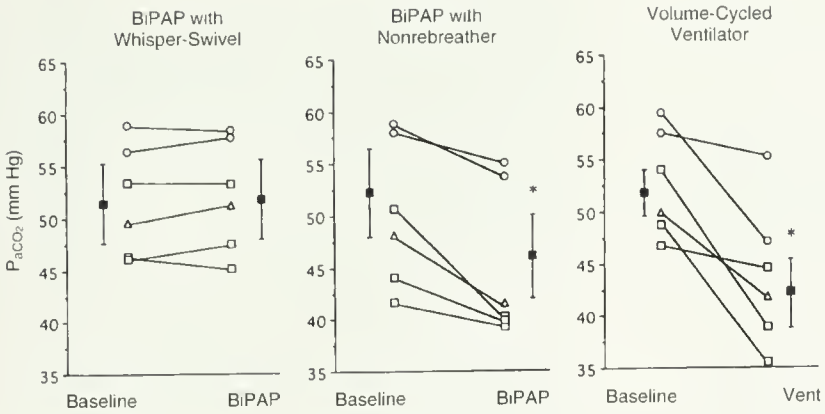

Fig. 9. P_{aCO_2} obtained at baseline and following 1 hour of ventilatory assistance with each of 3 ventilation methods. □ = chronic obstructive pulmonary disease; ○ = restrictive chest wall disease; △ = central alveolar hypoventilation patient; ■ = Mean (SEM). *$p < 0.005$ compared with resting values and with BiPAP ventilatory assistance using the Whisper-Swivel exhalation device. (Reprinted from Reference 26, with permission.)

Ideal Portable PTV

Although I do not believe these devices as currently designed have a place in the management of patients with acute ventilatory failure or in patients who require continuous ventilatory support, this does not mean that I believe these devices ventilate patients ineffectively. As shown in the data reviewed, these ventilators are capable of meeting the ventilatory demands of patients. Many of the current devices provide gas to spontaneously breathing patients much better than many ICU ventilators. The limitations outlined can be easily corrected. Appropriate exhalation mechanisms can be designed and mechanisms for attachment to high pressure gas sources developed or reservoirs added to increase and maintain more constant oxygen concentrations. Ability to operate these devices by backup batteries can be developed for use during long-term ventilatory support. Most importantly, devices can be fitted with alarms and appropriate monitors. All of these devices, if they are to be utilized in the management of acute respiratory failure must have alarms that identify large system leaks, disconnection, and mechanical failure of the ventilator. Considering the design of the ventilator, a high-pressure alarm is generally unnecessary but monitoring of V_T and rate is essential if they are to be used in acute respiratory failure. If ventilators are going to incorporate controls that contour the delivery of a pressure-targeted breath (eg, rise time and end-inspiratory trigger sensitivity), visual displays of airway pressure and flow are necessary for practitioners to properly adjust these controls. I anticipate that the design of the next generation of portable PTVs will eliminate these deficiencies. At that time, portable PTVs will come into common use to provide NPPV during acute respiratory failure.

PRODUCT SOURCES

Ventilators:

BiPAP STD30 and STD 20, Respironics, Murrysville PA
ARM-25 and DP90, Taema, Antony Cedex, France)
7200ae, 335, and 320 I/E, Nellcor Puritan Bennett, Lenexa KS
O'NYX, Pierre Medical Verrieres Le Buisson, France
VPAP, ResCare Inc, San Diego CA
Ventil+, SEFAM, Nancy, France
Quantum, Healthdyne, Marietta GA

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NPPV: Face versus Interface

Robert E Turner RRT

Introduction
The Interface
Face Mask versus Nasal Mask
Controlling Leaks
CO_2 Rebreathing
Connecting the Mask
Mask Placement & Patient Comfort
In Summary

Introduction

History has shown that many methods, once tried and set aside when other 'better' means emerged, may resurface and be found to be more useful than previously thought. Technologic advancement and renewed public interest or need can be the catalysts to revive discarded ways.

Such a cycle has been noted recently with the revival of noninvasive positive pressure ventilation (NPPV) in the acute and chronic respiratory patient population. Mask ventilation has, in some instances, become a first-line intervention in emergency rooms and in the critical care units.[1]

A 1992 publication[2] cites one of the earliest descriptions of NPPV, the work by Dräger in 1911. Dräger developed a tight-fitting mask coupled with a compressed gas source (the Pulmotor) to help resuscitate drowning victims. Later this device was used by policeman and firemen to assist civilians.[2,3]

In 1937 and 1938, Barach and his colleagues[4-6] reported their clinical experience in treating pulmonary edema continuous positive airway pressure applied with a mask. They described the beneficial effect of applying positive pressure to the airways during the breathing cycle to reduce the resistance in the conducting airways and the decreased lung compliance experienced by patients with congestive heart failure.

The Interface

Face Mask versus Nasal Mask

Success and failure in the use of NPPV has varied among investigators. Some find the face mask more effective while others have shown greater success with the nasal mask. Meduri and co-workers successfully avoiding intubation in approximately 72% of 197 patients studied.[7] Table 1 summarizes the studies published from 1989-1996,[8-31] including the work of Brochard et al[10] who also found face masks effective—perhaps due to the short duration of NPPV in patients studied.

To ventilate the patient as effectively as possible and to ensure maximum comfort, the clinician must use a mask that fits properly. Therefore, I believe that the interface—the mask and type of harness—can play just as important a role in determining the effectiveness of NPPV as does the ventilator. Proper sizing and fitting of the mask may require several attempts to accommodate facial architecture. A variety of masks are now available, and manufacturers continue to improve mask design and to develop gauging tools to help the clinician determine the proper size mask to use.

Choosing the correct mask style—facial or nasal—and size can be as challenging for the patient as for the clinician. The clinician has choices related to variations in style and size of

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Table 1. Studies Reporting Experience with Noninvasive Positive Pressure Ventilation

Authors, Year	n	Mask Type		Outcome	
		Facial	Nasal	Success	Failure
Meduri et al, 1989[8]	10	10	—	7	3
Elliott et al, 1990[9]	6	—	6	4	2
Brochard et al, 1990[10]	13	13	—	12	1
Marino, 1991[11]	12	—	12	8	4
Hodson et al 1991[12]	6	6	—	5	1
Meduri et al, 1991[13]	18	18	—	13	5
Chevrolet et al, 1991[14]	6	—	6	3	3
Pennock et al, 1991[15]	29	—	29	22	7
Benhamou et al, 1992[16]	30	—	30	18	12
Wysocki et al, 1993[17]	17	17	—	8	9
Bott et al, 1993[18]	30	—	30	26	4
Vitacca et al, 1993[19]	29	29	—	24	5
Fernandez et al, 1993[20]	12	12	—	9	3
Pennock et al, 1994[21]*	110	—	110	64	46
Soo Hoo et al, 1994[22]	12	—	12	5	7
Meduri et al, 1994[23]	11	11	—	7	4
Tognet, 1994[24]	15	7	8	6	9
Confalonieri et al, 1994[25]	28	—	28	18	10
Wysocki et al, 1995[26]	21	21	—	8	13
Kramer et al, 1995[27]	16	—	16	11	5
Sachetti, 1995[28]	22	—	22	20	2
Ambrosino et al, 1995[29]	59	25	34	46	13
Brochard et al, 1995[30]	43	43	—	32	11
Meduri et al, 1996[31]	158	158	—	112	46
Total	713	370 (52%)	343 (48%)	488 (68%)	225 (32%)

* Includes 29 patients from Pennock 1991 study

mask and head harness to accommodate different facial contours and architecture (Table 2).

The mask 'cushion,' which comes in contact with most of the face, should be of a nonallergenic soft, supple material—not hard plastic—to minimize the likelihood of pressure necrosis. The shell or dome should be made of a clear material, so

Table 2. Interfaces Available for Noninvasive Positive Pressure Ventilation (1995)

Manufacturer & Location	Design	Sizes	Harness Type*	Single Use or Reusable?
Ambu®, Linthicum MD	Face (2 styles)	6 of 1; 5 of other	Elastic	Single
Baxter Round Lake IL	Face (2 styles)	3 of each style	Elastic	Single
Bird®, Palm Springs CA	Face	3	Elastic	Single
Gibeck, Indianapolis IN	Face	3	Elastic	Single
Hospitak, Farmingdale NY	Face (2 styles)	3 of each style	Elastic	Single
Hans Rudolph, Kansas City MO	Face	8	Polyester head cap	Reusable
Healthdyne Soft Series, Marietta GA	Nasal	7	Crown strap	Reusable
Intertech/Sims, Keen NH	Face	2	Elastic	Single
King System Corp, Noblesville IN	Face	6	Elastic	Single
LifeCare, Westminster CO	Nasal	7	Elastic	Reusable
MED Systems®, Santa Monica CA	Face	3	Elastic	Single
Nellcor Puritan Bennett, Carlsbad CA	Face	3	Elastic	Reusable
ResCare Sullivan® Bubble, San Diego CA	Nasal (3 series)	5 in each series	4 types of headcap	Reusable
Respironics, Murrysville PA	Nasal (2) & Face (1)	8 nasal, 4 face	Headcap or straps	Reusable
Rüsch, Duluth GA	Face (4 styles)	1 of 1; 2 of 2; 3 of 1	Elastic	Reusable
Vacumetrics, Ventura CA	Nasal & face	5 nasal; 5 face	Foam-cushioned cap, Velcro straps	Reusable
VENTLAB Corp, Mocksville NC	Face	3	Elastic	Single
Vital Signs, Totowa NJ	Face	3	Elastic	Single

that the patient can be observed for excessive secretions or vomitus. The harness or headgear should also be made of either a soft cloth or a nonallergenic elastic material.

Claustrophobia may make the patient unable to tolerate NPPV, especially if a full face mask is used. Some patients may tolerate a nasal mask better than a face mask. Nasal masks are thought to minimize the potential complication of aspiration, and they facilitate oral intake and allow easier expectoration.[7]

The nasal mask is widely used. However, one should remember that when the resistance of the nasal passages is added to the abnormal airway resistance present in many patients in acute respiratory failure, the ventilator may be unable to provide the pressure necessary to overcome that total resistance. It is widely held that the nasal passages contribute ≥ 50% of normal airway resistance.

The face mask provides less resistance than the nasal mask but does not allow oral intake or expectoration. The potential for aspiration is increased, and, therefore, the face mask should be made of a clear material. Meduri et al[1] published an account of their success using a face mask in 158 patients with various disease and varying degrees of respiratory failure. Effective response within 2 hours after initiation of NPPV with a face mask predicted eventual success ($p < 0.0001$).[1] Considering the dyspnea Meduri's study population experienced, the response may be attributed to the fact that many dyspneic patients are mouth breathers, and the nasal mask facilitates only nose breathing. Nasal masks have been reported to be ineffective when nasal resistance is > 5 cm $H_2O \cdot s \cdot L^{-1}$.

Sinusitis or any deviation of the turbinates contributing to increased resistance may also be a factor when one is choosing the proper interface. When such conditions are present, the choice of a mask that will cover the mouth and the nose (face or oronasal mask) may be appropriate. Some patients who use the face mask in their acute phase may graduate to the nasal mask. In mild respiratory failure, the nasal mask can be tried first. If it is not successful, a face mask can be applied. Fitting a face mask on patients without teeth or dentures in place or on bearded patients can be difficult, and a nasal mask may be the better choice.

Controlling Leaks

A good seal (obtained without securing the mask too tightly) is imperative. One should keep in mind that slight leakage around the mask during inspiration is not harmful. However, the leak must not be so large as to interfere with the ventilator's cycling from inspiration to expiration and from expiration to inspiration. The exhaled tidal volume or the estimated inspired tidal volume is a key indicator of adequate ventilation. Too great a leak can be detected from the flow-time curve on a graphics screen (if the ventilator is so equipped), by measuring the exhaled tidal volume, or from the actuation of the low-PEEP (ie, positive end-expiratory pressure), low-inspiratory pressure, or disconnect alarm. Careful setting of the ventilator's alarms can adjust for optimum sensitivity once the patient is considered in synchrony and stable with the settings.

Many clinicians are trained to note any leaks within a circuit during mechanical ventilation and to take steps to eliminate the leak. Therefore, the tendency to overcompensate by tightening the mask to seal off the leak may attribute to some mask intolerance.

Today's technology has almost eliminated the concern for leaks that in the past were considered a compromise to adequate ventilation. Manufacturers have microprocessing logic within the design of ventilatory devices that recognizes leaks and adjusts flow to maintain prescribed levels of ventilation. Nevertheless, a gross leak requires attention to the adjustment, size, or type of mask being used or to the level of pressure ventilation.

CO_2 Rebreathing

Nasal masks have about 105 mL of dead space whereas face masks have about 250 mL, causing CO_2 rebreathing to be a concern.[7] To my knowledge, of all reported investigations to date, there have been no reports of CO_2 rebreathing related to the dead space of the mask. However, the amount of end-expiratory pressure set on the machine and the resistance of the circuit expiratory port or the mask expiratory port does play an important role in CO_2 rebreathing.

To alleviate this potential problem end-expiratory pressure > 8 cm H_2O was advocated by Ferguson and Gilmartin.[32] Also a nonrebreathing valve designed for specific use in NPPV was effective but could cause higher expiratory resistance. Lofaso et al[33] found that levels of end-expiratory pressure < 2 cm H_2O and incorporation of a nonrebreathing valve reduced the rebreathing effect. But, increased expiratory resistance and increased external PEEP decreased the actual amount of inspiratory pressure support and, therefore, increased the work of breathing twofold.[32,33]

Connecting the Mask

Once the best available mask is chosen, connection to the ventilator is similar to connecting an endotracheal tube. Of particular interest is the way the harness is attached to the mask. Some masks have prongs (studs on the mask where the harness is secured). These prongs are often referred to as either peripheral or central prongs. The peripheral prongs are on the outer edge of the mask and when the harness is attached, even distribution of pressure over the surface area of the face is achieved.[8] These prongs are found on orofacial masks but not on most nasal masks. Nasal masks have holes on both sides where hooks from the harness or headgear can be attached. These holes allow the clinician to make adjustments to facilitate a better seal. Some nasal masks also have loops through

which headgear straps can be passed, similar to the belt loops on trousers or skirts.

The central prongs allow the mask to be attached at the center of the mask via holes on the harness. Although, in my experience, attachment to central prongs can be effective in some patients, the central location may not allow for even distribution of pressure over the surface of the face. When the harness is attached to central prongs, it is sometimes necessary to cross the straps (ie, the top strap to the bottom prong and the bottom strap to the top prong). This method tends to keep the straps from migrating into the eyes of the patient.

Mask Placement & Patient Comfort

I have found that a cushion for the forehead and a soft wound-care dressing, such as Duo-Derm® (Bristol-Myers Squibb, Princeton NJ) or Restore® (Hollister, Libertyville IL), for the nasal bridge reduces pressure and/or leaks from the nose when a nasal mask is used. However, this application is optional and may be done when the patient is clinically stable and rested enough to briefly remove the mask.[7] Redness of the skin may develop, but breakdown of the skin usually takes several hours The skin should be checked daily for any signs of abrasion or necrosis. Supplemental O_2 is provided via cannula or oxygen mask during the inspection.

I have found that placing the harness behind the patient's head prior to application of the mask saves unnecessary manipulation once the patient is ready to secure the mask. The mask should be held gently on the patient's face until he or she is in synchrony with the ventilator and comfortable with the feel of the ventilatory assistance delivered. The clinician should continue to provide explanations and reassurance to the patient at all times.

Once the patient is comfortable, the pressure should be titrated to optimum therapy and comfort. This should be done early in the therapy process with special attention to the cycling (inspiration and expiration) of the ventilator. With the patient comfortable and with the ventilator cycling appropriately, the mask can be secured with the harness, avoiding a tight fit. The patient's comfort is very important to the effectiveness of mask ventilation.[7] Once secure, the mask may be gently readjusted as needed. Placing the mask too high into the eyes can lead to conjunctivitis and placing it too low below the chin can lead to leaks around the mandible. The clinician should be able to pass one or two fingers easily between the harness and the patients face after attaching the harness to the mask.

In Summary

As clinicians utilize NPPV as an alternate mode of mechanical ventilation, it is important that advances be made in mask design. Continued research in the clinical setting is needed to develop more appropriately designed interfaces. Much time and effort has been spent in developing the ventilator and now the time for attention to the face versus the interface should proceed.

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Continuous and Periodic Applications of Noninvasive Ventilation in Respiratory Failure

Richard G Wunderink MD and Nicholas S Hill MD

CONTINUOUS NPPV FOR ACUTE RESPIRATORY FAILURE
- Introduction
- Study Design
  - Point of Intervention
  - Relevant Outcomes
- Results of Randomized Studies
  - Mortality
  - Intubation
  - Duration of Ventilation
  - Complications
- Conclusions
  - Level-I Evidence
  - Qualification Regarding Results
- Further Research
  - Disease Categories
  - Other Outcomes
  - Exclusion Criteria
  - Methods of Providing NPPV
  - Monitoring
  - Other Research
- In Summary

NOCTURNAL NPPV FOR CHRONIC RESPIRATORY FAILURE
- Introduction
- Neuromuscular & Chest-Wall Disorders
- Chronic Obstructive Pulmonary Disease
- In Summary

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CONTINUOUS NPPV FOR ACUTE RESPIRATORY FAILURE

Introduction

Noninvasive positive pressure ventilation (NPPV) has been used in patients in acute respiratory failure from a variety of causes. Reports of the number of patients and types of underlying disorders treated are increasing almost monthly. A list of the causes of acute respiratory failure for which NPPV has been attempted is seen in Table 1.[1] By far the largest number of patients and best data exist for acute exacerbation of chronic obstructive pulmonary disease (COPD).[2-5]

Table 1. Causes of Acute Respiratory Failure for which Noninvasive Positive Pressure Ventilation Has Been Attempted*

Acute exacerbation of chronic obstructive pulmonary disease
Acute respiratory distress syndrome
Asthma
Atelectasis
Cystic fibrosis
Community-acquired pneumonia
Hypoventilation syndromes
Obstructive sleep apnea
Obesity hypoventilation syndrome
Lung cancer
Near-drowning
Neuromuscular disease
Pneumocystis carinii pneumonia
Postoperative respiratory insufficiency
Postextubation stridor or failure
Pulmonary edema of cardiac origin
Pulmonary embolus
Restrictive lung disease
Trauma
Upper airway obstruction

*Adapted from Reference 1, with permission.

With the proliferation of studies and indications, review of the evidence for the effectiveness of NPPV is appropriate. Most published studies unfortunately consist of uncontrolled case series, historical control studies, or case reports. Although blinding is impossible with NPPV, randomization can be accomplished. Four randomized control trials have been reported. This includes 2 trials in acute exacerbation of COPD,[2,3] 1 trial in acute respiratory failure other then COPD,[6] and 1 trial with a mixed population of COPD and non-COPD patients.[4]

Study Design

Before reviewing the results, we want to discuss several issues regarding study design.

Point of Intervention

The point of intervention with NPPV can occur at one of three different times. The best studied is prevention of acute respiratory failure,[2-6] as defined by need for intubation and mechanical ventilation, in a group of patients at high risk for mechanical ventilation. These studies look at prophylactic treatment. Because the intervention is prophylactic, not all control patients will be intubated and some patients in the treatment group will undergo NPPV unnecessarily.

The second point of intervention is at the time that acute respiratory failure has occurred, and, in that situation, NPPV is treatment rather than prevention. Despite their titles, most studies of NPPV have actually excluded patients who need immediate intubation.[2-4,6] Therefore, the data on actual treatment of acute respiratory failure are less convincing. The study end point is different when treatment is truly being studied. Comparing the incidence of intubation is no longer appropriate because, by definition, all control patients should require intubation. Other end points such as duration of mechanical ventilation, incidence of complications, and mortality are more appropriate.

Distinguishing the point at which the intervention switches from prevention to treatment is subjective. This limits the applicability of a study's results to an individual practitioner. Yet this distinction may be critical in the success of NPPV. In the study by Brochard et al,[2] 23 of the 31 control-group patients who required intubation were intubated within 3 hours of randomization despite an exclusion criteria for study entry of "need for immediate intubation." Other attempts to use a set of objective criteria to distinguish between acute respiratory failure requiring immediate intubation and acute respiratory insufficiency in COPD patients did not define a population at increased risk of subsequent intubation or mortality.[5]

The third interesting and potentially beneficial point of intervention with NPPV is either for salvage of extubation failures[5] or for accelerated weaning from mechanical ventilation. Although such patients have been included in case series, no randomized study has addressed this indication.

Relevant Outcomes

The assumption in most of the studies has been that avoidance of endotracheal intubation is the appropriate and most beneficial goal. This assumption is appropriate only if mortality and other complications are also the same or lower. Whether avoidance of endotracheal intubation alone is better if all other factors, including mortality, length of stay, complications, and cost, are equal is a subjective decision to be made by the patient and has not been studied. We have observed a few patients who, having had experience with NPPV, subsequently elect endotracheal intubation rather than repeating attempts at NPPV.

Mortality is clearly an appropriate outcome variable. While comparison of mortality between NPPV and conventional treatment is the primary consideration, excess mortality in the control group may indicate a selection bias. Because patients at highest risk (based on the need for immediate intubation) have been excluded from some studies, the mortality of randomized studies of NPPV should have a control mortality rate at or below the mortality rate from epidemiologic studies for patients with that cause of respiratory failure.[7]

The duration of mechanical ventilation and the corresponding need for intensive care monitoring is also an important outcome variable. Because duration of mechanical ventilation drives most of the charges for patients with acute respiratory failure, this outcome may be an easy surrogate for cost of care.[2,4,7,9] Although the cost of providing NPPV does not appear to be higher than the cost of traditional mechan-

ical ventilation, many hospitals still charge the same rate for mechanical ventilation whether delivered via mask or endotracheal tube.[4,10]

One of the major outcomes hypothesized to favor NPPV is the complication rate. The trade-off between the incidence of laryngotracheal injury and facial pressure necrosis is not the only comparison. Avoidance of other important complications, such as development of nosocomial pneumonia or sinusitis, aspiration, and inability to handle secretions, are probably as important but often are more difficult to assess, either because of difficulties in diagnosis or because other independent risk factors may not be evenly distributed between noninvasive and invasive applications. A critically important aspect of analysis is whether failure of NPPV leads to greater complications than if the patient had been intubated originally. A worse outcome in a subgroup of patients who fail NPPV may be hidden if a majority are successfully treated.

Results of Randomized Studies

The results of the 4 randomized controlled trials that have been published are summarized in Table 2.

Mortality

The largest study published to date (1996) is the multicenter study of Brochard et al[2] using a nasal mask and pressure support ventilation for patients with acute exacerbations of COPD. The relative risk of death was 0.44 (95% confidence interval [CI] 0.18-1.06). This corresponds to a relative risk reduction of death of 67% compared with controls. The number needed to treat (NNT) with NPPV to avoid 1 death is only 5 patients. Two other randomized, controlled studies also included COPD.[3,4] The trend toward decreased mortality was consistent through the 3 studies, although decreased mortality was significant only in the Brochard study.[2] Bott et al showed an almost identical trend toward decreased mortality, although the smaller numbers precluded statistical significance.[3] The mortality in both control groups was not excessive compared to the 31.8% mortality for ventilated COPD patients found in recent multicenter studies.[7] Bott et al did demonstrate a center effect, with one center having significantly lower mortality than the other two.[3] The study by Kramer et al,[4] which included primarily patients with exacerbations of COPD (23/31, 74%), did not find a significant difference in mortality but had a lower overall mortality for both NPPV and control patients.

The study of Wysocki et al[6] is the only study that specifically studied patients without COPD. They found no difference in mortality for the entire group. However, a subgroup of patients with elevated P_{aCO_2} (> 45 torr) at the time of randomization suggested a trend toward decreased mortality. When the subgroup without CO_2 retention is analyzed, an insignificant trend toward increased mortality with NPPV is noted.

Intubation

The incidence of endotracheal intubation in patients with COPD was significantly lower in the study of Brochard et al[2] with a relative risk 0.35 (95% CI 0.21-0.60). This corresponds to a relative risk reduction of intubation of 65% compared with controls. The NNT with NPPV to avoid 1 intubation is only 2 patients. Kramer et al[4] found a similar significant reduction in the incidence of intubation, both in the overall group and in the COPD subgroup.

For non-COPD patients, the benefit of NPPV in avoidance of intubation is not clear. Wysocki et al[6] found no overall difference in the incidence of intubation. The subgroup of patients

Table 2. Results of Randomized Controlled Trial of Positive Pressure Ventilation Patient Group

Patient Condition	Interface	Mode of Ventilation	End Point	Patient Group		Relative Risk Reduction (%)	Relative Risk	No. Needed to Treat	p Value
				Treatment	Control				
COPD[3]	Nasal	Volume	Death	3/30 (0.10)	9/30 (0.30)	66.7	0.20	5	0.11
COPD[2]	Facial	Pressure Support	Death	4/43 (0.09)	12/42 (0.29)	69.0	0.20	5	0.02
Mixed[4]	Nasal	Bi-level	Death	1/16 (0.06)	2/15 (0.13)	53.8	0.07	14	0.60
Mixed (no COPD)[6]	Facial	Pressure Support	Death	7/21 (0.33)	10/20 (0.50)	34.0	0.17	6	0.46
PaCO2 > 45 torr*	Facial	Pressure Support	Death	1/11 (0.09)	4/6 (0.67)	86.6	0.58	2	0.06
PaCO2 ≤ 45 torr*	Facial	Pressure Support	Death	6/10 (0.60)	6/14 (0.43)	−34	−0.17	6	0.76
COPD[2]	Facial	Pressure Support	Intubation	11/43 (0.26)	31/42 (0.74)	64.9	0.48	2	0.001
Mixed[4]	Nasal	Bi-level	Intubation	5/16 (0.31)	11/15 (0.73)	57.5	0.42	3	0.05
COPD*	Nasal	Bi-level	Intubation	1/11 (0.09)	8/12 (0.67)	86.6	0.58	2	0.017
Mixed: No COPD[6]	Facial	Pressure Support	Intubation	13/21 (0.62)	14/20 (0.70)	11.4	0.08	14	0.88
PaCO2 > 45 torr*	Facial	Pressure Support	Intubation	4/11 (0.36)	6/6 (1.0)	64.0	0.64	2	0.02
PaCO2 ≤ 45 torr	Facial	Pressure Support	Intubation	9/10 (0.90)	8/14 (0.57)	−57.9	−0.33	3	0.17
COPD[2]	Nasal	Pressure Support	Complications	7/43 (0.16)	20/42 (0.48)	66.7	0.32	3	0.001

*Subgroup analysis

with CO_2 retention again showed benefit, but the remaining patients had a higher incidence of intubation when randomized to NPPV. The non-COPD patients in the study of Kramer et al[4] also did not appear to benefit from NPPV.

Duration of Ventilation

Information regarding the duration of ventilation is complicated by the differential incidence of intubation and nonstandard reporting. Only Kramer et al[4] directly report the duration of ventilator use. They found no significant difference between groups (8.8 ± 3.9 days for controls vs 8.7 ± 3.6 for NPPV), even in the COPD subgroup. In the studies of Kramer et al[4] and Brochard et al,[2] patients who failed NPPV and required intubation had a longer duration of ventilation than intubated control patients.

Duration of ICU stay or duration of hospital stay may serve as a surrogate for duration of ventilation. Brochard et al[2] found a significantly longer duration of hospital stay in the COPD control population while Wysocki et al[6] found a nonsignificant increase in ICU length of stay in non-COPD controls. Kramer et al[4] found no increase in hospital stay in their control population.

Complications

Brochard et al[2] prospectively determined the incidence of a variety of complications and found that NPPV in COPD was associated with a relative risk of 0.42 (95% CI 0.21-0.82) for complications.

Conclusions

Level-1 Evidence

Based on standard guidelines to distinguish useful from useless or harmful therapy, Level-1 evidence of efficacy for NPPV in prevention of respiratory failure and death in COPD patients exists.[11,12] Three randomized control trials,[2-4] with a total of 176 patients, several other randomized control trials published in abstract form, and a consistent pattern in nonrandomized studies,[1,8] support efficacy. The differences between NPPV and control patients are clinically relevant and statistically significant. To prevent 1 death in COPD patients, the NNT ranges from 5-15 patients. The NNT to prevent intubation and mechanical ventilation is only 2 to 3 patients.

In contrast, no Level-1 evidence exists for the benefit of NPPV in non-COPD patients. The group studied by Wysocki et al[6] was heterogeneous and potential benefit in subgroups may be present. The benefit found by Wysocki et al in the subgroup of patients with an elevated P_{aCO_2} needs to be prospectively studied. Prospective randomized studies of other more homogeneous groups, based on factors such as cause of acute respiratory failure, need to be performed before NPPV can be accepted for these disorders. Although the underlying cause of acute respiratory failure (eg, cardiogenic pulmonary edema, pneumonia, laryngeal obstruction) did not distinguish between success and failure in the study of Wysocki et al,[6] other series suggest better results in certain groups.

Qualifications Regarding Results

Several important criticisms of the Brochard et al[2] can be voiced. Only 31% of COPD patients were actually randomized. A study by Meduri's group[5] also found that only approximately 24% of patients had a trial of NPPV when used as first-line therapy for acute respiratory failure. Therefore, although NPPV was successful in the patients studied, a large subgroup of COPD patients was excluded. In addition, only 59/85 (69%) of the patients in Brochard's study received β-agonist bronchodilators, which should be first-line therapy in patients with acute exacerbation of COPD. Of the patients studied, 24% were intubated within the first hour, despite the exclusion criteria of need for immediate intubation. Of all candidates, 27% had already been excluded for this reason. The control group contained a disproportionate number of patients intubated within the first hour. Also, the mean duration of ventilation was excessive in the patients who were intubated.[7,9] Control patients were ventilated for 17 days compared to 25 days for NPPV failures.

Brochard et al[2] did note a higher Simplified Acute Physiology Score (SAPS) in patients who were failures. A high-risk subgroup of patients may exist that would be predicted to have a prolonged duration of mechanical ventilation. Seneff et al[9] has demonstrated that the Acute Physiologic Score, which is similar to the SAPS score, contributes 25% of the variability in duration of mechanical ventilation of all intubated patients. An additional 10% is predicted by other disease-specific variables, such as P_{aCO_2}, respiratory rate, and P_{aO_2}/F_{IO_2}. Because the underlying disease contributed to 44% of the variability, the SAPS and other acute physiology scores may have even greater value for predicting the duration of mechanical ventilation in a population with a single cause of respiratory failure, such as that of Brochard et al.[2] Therefore, patients with more severe illnesses as reflected by SAPS or APACHE scores would be predicted to have higher duration of mechanical ventilation.[9]

In the study by Kramer et al,[4] the duration of ventilation was more appropriate with controls receiving 6.4 days of mechanical ventilation and NPPV patients receiving 7.6 days of intervention. This is more consistent with the APACHE III database.[7] It is interesting to note that length of stay was not significantly different between patients who received NPPV and those randomized to standard therapy and that hospital charges were equal. Bott et al[3] also found that the length of stay was not significantly different. Patients were discharged on NPPV in several studies, confounding anal-

ysis of duration of ventilation. The significant center effect found in the study of Bott et al[3] suggests that either familiarity with NPPV or different patient populations can affect the benefit of NPPV.

Further Research

Disease Categories

Substantial unresolved issues regarding NPPV in COPD patients remain. The present data clearly suggest that some subgroups of patients may be more responsive to NPPV than others. Patients suffering from depressed respiratory drive, whether on the basis of hypercarbic encephalopathy or extrinsic respiratory depressants, probably can be successfully treated with NPPV. In addition, patients in whom work of breathing is excessive, either from airway obstruction or the mechanical disadvantages caused by auto-PEEP,[13] should improve with the NPPV. It is unclear whether NPPV allows adequate rest for respiratory muscles if the patient has progressed to the point of true fatigue. This may explain some of the prolonged ventilation in patients who are NPPV failures.[2] It is also unclear whether mask CPAP alone would have the same results as has NPPV. Mask CPAP has had an 81% success rate in small studies of COPD patients,[1] possibly related to decreased work of breathing and relief of auto-PEEP.

Observational studies of specific subgroups other than COPD including asthma,[14] postoperative respiratory failure,[15,16] congestive heart failure/cardiogenic pulmonary edema,[17] community-acquired pneumonia,[5] and postextubation respiratory failure[5] have been published. There are limited case control and cohort data among these, but randomized control trial of these specific disease categories are lacking. Preliminary results of several randomized trials have been presented, so further clarification of the benefit of NPPV in specific disease categories other than COPD should be forthcoming.

For non-COPD patients, comparison trials with mask CPAP are even more important. Two Level-1 studies of mask CPAP in cardiogenic pulmonary edema demonstrated a significant benefit.[18,19] In contrast, a preliminary report of NPPV in cardiogenic pulmonary edema suggested increased risk of myocardial infarction in patients randomized to NPPV.[20] Therefore, prospective randomized studies of mask CPAP versus NPPV are mandatory if NPPV is shown to be of benefit in this disorder.

The use of NPPV in patients who have chosen not to undergo endotracheal intubation is an additional issue. Several patients in randomized studies elected to forgo intubation despite the need for this support.[3] Case series show that many of these patients can be adequately ventilated temporarily.[5] Despite this, a substantial number of these patients subsequently die during that hospitalization, and the inappropriate use of NPPV may add significantly to the cost of terminal care.[21]

Other Outcomes

Probably the most important unresolved issue is the cost-effectiveness of therapy. Despite avoiding intubation and mechanical ventilation, the cost may not be significantly different.[4] Although time spent by the respiratory therapist is probably not greater for NPPV than for invasive ventilation,[4] it probably is not less. Because not all control patients are intubated, the use of NPPV may increase the amount of time involved in the care of patients.

Other reported benefits of NPPV need to be studied prospectively. In particular, the lower incidence of pneumonia reported in several studies may be unrelated to NPPV. NPPV appears to be most beneficial in patients who are expected to have a short duration of mechanical ventilation even if intubated. Because nosocomial pneumonia is clearly dependent on the duration of mechanical ventilation,[22] the decreased incidence of pneumonia found in NPPV may relate only to selection of patients who would otherwise have short-term intubation and mechanical ventilation.

Exclusion Criteria

Exclusion criteria for the use of NPPV, other than disease category, have not been well developed. Two levels of exclusion can be suggested from the literature and are shown in Table 3. Most of the studies that have demonstrated benefit have excluded patients who have a need for immediate intubation. Although the definition of need for immediate intubation is nebulous, it appears to be an important predictor of the success of NPPV. Almost all investigators suggest that an uncooperative patient is a poor candidate for NPPV. The presence of facial trauma or burns and the need for airway protection appear to be relatively absolute exclusions for NPPV. Hemodynamic instability with either hypotension or dysrhythmia is a near-absolute contraindication to NPPV and falls in the category of need for immediate intubation.

Table 3. Contraindications to Noninvasive Positive Pressure Ventilation

Absolute Contraindications
Need for immediate intubation
Hemodynamic instability
Uncooperative patient
Facial burns
Facial or skull trauma
Need for airway protection
Relative Contraindications
Extreme anxiety
Excessive secretions
Massive obesity
Most adult (acute) respiratory distress syndrome patients

A second level of relative exclusion criteria is suggested from the literature but needs validation in prospective stud-

ies. Extreme anxiety may be related to the sense of dyspnea. A trained team approach and, rarely, the use of short-acting sedatives might allow these patients to be successfully treated with NPPV. Excessive secretions are also a relative contraindication because of the difficulty of coughing against positive pressure. Patients have either been excluded based on the presence of excessive secretions or unsuccessful treatment with NPPV has been blamed on excessive secretions. Use of full face masks may lead to more problems with secretions than does the use of nasal masks, but this has not been studied prospectively. Massive obesity is suggested to be a relative contraindication. However, the extensive experience with nasal CPAP in patients with obstructive sleep apnea suggests that obesity may not be an absolute contraindication and that careful titration may in fact allow successful use of NPPV. Among non-COPD causes of acute respiratory failure, patients with acute respiratory distress syndrome (ARDS) have routinely done poorly. Because the average duration of mechanical ventilation for ARDS patients is ≥ 10-14 days, NPPV should not be attempted unless a rapidly reversible form of ARDS, such as uncomplicated fat emboli syndrome or leukoagglutinin transfusion reactions, is present.

Methods of Providing NPPV

Successful NPPV has been accomplished with both nasal[3,4,15,16] and full face masks[2,5,6,8,23] and with both volume-cycled[3,23] and pressure-cycled ventilators.[2,4-6,8,15,16,23] A small randomized study[23] suggests that pressure-cycled ventilation may be equally efficacious and better tolerated. A randomized study of nasal versus full face mask ventilation is clearly needed.

Weaning from NPPV can follow one of two methods. Either progressively longer periods of time off NPPV or a progressive decrease in the pressure support level can be used. This has not been prospectively studied. Weaning methods may depend on the underlying disease and reason for respiratory failure. A progressive decrease in pressure support level may be more important for patients who have hypoxic failure or causes other than COPD. If the underlying problem and the potential need for invasive mechanical ventilation are relieved in a short period of time, weaning from NPPV may significantly prolong ICU stay. Conversely, NPPV has been shown in uncontrolled studies to salvage patients who are extubation failures.[5]

Monitoring

The criteria for failure or success of a trial of NPPV have not been prospectively identified. Our group[5] found that success correlates with improvement in an arterial blood gas value, particularly a drop in P_{CO_2} 1-2 hours after initiation of NPPV. Kramer et al[4] found much slower improvements in blood gas values, even in successful trials of NPPV. Respiratory rate also appears to be a significant predictor of the success of noninvasive ventilation. Patients whose respiratory rate drops into the low 20s or less are likely to have a successful trial of NPPV. The exhaled tidal volume may be an important predictor of success. Brochard et al[8] demonstrated that increasing the pressure support level to 20 cm H_2O resulted in significant increases in tidal volume and decreases in respiratory rate. Other criteria are patient comfort and synchrony with the ventilator. Inability to synchronize may actually increase work of breathing and auto-PEEP. Synchrony can be assessed only at the bedside by trained observers. The leak from the mask should also be monitored, particularly with the use of pressure support. If a considerable leak occurs, the pressure support off-triggering mechanism may not be activated, and the patient essentially experiences CPAP at the set level of pressure support.

Prospective studies of possible predictors of success and appropriate timing of NPPV are needed. Determination of indicators of the need to abort a trial of NPPV and intubate the patient may avoid the prolonged ventilator dependence of NPPV failures found in some studies. In addition, further studies are needed to determine the appropriate target measurement (blood gas values, respiratory rate, or exhaled tidal volume) and level for titration of NPPV.

The level of monitoring required determines the sites at which NPPV can be provided. NPPV has been successfully performed in step-down units as well as in intensive care units. The requirements for sophisticated monitoring suggest that NPPV not be performed in a routine care area of the hospital unless the level of support and expertise of respiratory care practitioners allows the necessary monitoring. Requirements for higher levels of care affect the cost-effectiveness of NPPV.

Other Research

Several additional reported benefits of NPPV need to be explored. Day et al[16] showed that rapid reversal of infiltrates visible on chest radiograph occurred with NPPV, suggesting that atelectasis had been present. However, once again, mask CPAP has already been proven to be a benefit in this condition in a randomized controlled trial.[24] Also, Pollack et al[25] have demonstrated increased bronchodilator delivery in a randomized controlled trial of NPPV in the emergency room. This factor may play a role in the demonstrated benefit in COPD patients.

In Summary

NPPV has been demonstrated to decrease the incidence of intubation and is associated with a lower mortality rate in patients with exacerbations of COPD. The use of NPPV for COPD exacerbations should no longer be considered experimental and can be considered appropriate for routine clinical practice in centers with expertise in its application.

At the present time, the benefit of NPPV remains to be proven in patients with impending respiratory failure from other causes. Although observational studies have reported

on NPPV in many of these disorders, at this time (1996), we need well-executed randomized trials designed to answer the question, Is NPPV better than endotracheal intubation and mechanical ventilation for these conditions? Completion and publication of several randomized studies already reported in preliminary form should begin to clarify other indications for NPPV.

Ongoing research is required on the appropriate delivery mechanisms for NPPV, exclusion criteria, and monitoring. The potential benefits of NPPV in acute respiratory failure appear to be great if the findings of uncontrolled studies are realized in randomized controlled trials.

NOCTURNAL NPPV FOR CHRONIC RESPIRATORY FAILURE

Introduction

One of the best established indications for NPPV is the use of nocturnal nasal ventilation for patients with chronic symptomatic hypoventilation. During the late 1980s, a number of studies were published supporting the effectiveness of this application.[26-37] None of these studies was controlled and most had few patients, but they consistently demonstrated improvements in daytime CO_2 retention, oxygenation, and symptoms, such as morning headache and daytime hypersomnolence. In these studies, nasal masks connected to portable volume-limited positive pressure ventilators were used.

Neuromuscular & Chest-Wall Disorders

The studies of the 1980s,[26-37] reported primarily the experience with slowly progressive neuromuscular disorders and chest-wall deformities. The unanimously favorable results led to a reluctance on the part of investigators to formulate randomized prospective trials, given the concern that this almost certainly effective therapy would have to be randomly withheld from ill patients who could be harmed by a delay in initiation. As an alternative approach, two groups of investigators temporarily withheld nocturnal nasal ventilation from patients who had previously been stabilized using it.[38,39] During the period of withdrawal, both groups demonstrated a deterioration in nocturnal gas exchange with reductions in oxyhemoglobin saturation, increases in transcutaneous carbon dioxide tensions, and worsening symptoms. This deterioration was reversed upon reinstitution of nocturnal nasal ventilation. One of the studies[39] also noted a deterioration in sleep quality upon withdrawal. These and the earlier uncontrolled studies have led to a general acceptance that nocturnal ventilatory assistance is effective in patients with symptomatic chronic respiratory failure due to neuromuscular disease or chest-wall deformity. Considering the greater ease of administration of NPPV and potential reduction in complication rates relative to invasive positive pressure ventilation, we believe that many practitioners consider NPPV the modality of choice for support of such patients who require only nocturnal ventilatory assistance and are capable of adequately protecting their airway.

Debate continues on the optimal time for initiation of NPPV for chronic respiratory failure and whether NPPV is as effective as invasive positive pressure ventilation in prolonging survival. One recent randomized prospective trial from France[40] examined the hypothesis that prophylactic initiation of NPPV, before the development of daytime CO_2 retention or symptoms, would slow the progression of neuromuscular disease. Patients with Duchenne muscular dystrophy were randomized to receive prophylactic nocturnal nasal NPPV or no ventilation. A surprising outcome of this study was the finding that mortality increased in the group using nasal ventilation. The authors surmised that the ventilator increased mortality by giving patients a false sense of security, causing them to delay seeking medical attention after developing respiratory infections and then succumbing to secretion retention. However, numerous flaws in the study raise doubts about the validity of these mortality findings. Nonetheless, we believe that few practitioners currently hold that prophylactic initiation of NPPV has any utility. Further, it has been our observation, and, we believe most practitioners agree, that attaining patient cooperation and compliance with the use of NPPV is difficult in the absence of symptoms.

The question of effects on long-term survival has recently been addressed in two large follow-up studies.[41,42] Both show excellent long-term results in patients with post-polio syndrome and kyphoscoliosis, but rates of NPPV continuation were much lower in patients with COPD. Although there was no unventilated control group in these long-term studies, the results compare favorably with those of a similar follow-up study performed by one of the same groups on patients treated with invasive positive pressure ventilation.[43] Thus it appears that NPPV is effective in assisting ventilation for the long term in appropriate patients, that survival is almost certainly prolonged, and that confirmatory controlled trials are likely never to be done.

Chronic Obstructive Pulmonary Disease

Results of studies on use of NPPV in patients with chronic respiratory failure due to COPD have been much more mixed than those on patients with restrictive thoracic disease. An early uncontrolled study[44] showed improvement in gas exchange and symptoms in 6 patients with chronic CO_2 retention due to COPD, but subsequent controlled studies have shown conflicting results. Strumpf et al[45] randomized 19 patients to receive ventilatory assistance using the BiPAP device via a nasal mask or standard therapy. Only 7 patients completed the 3-month crossover trial, with 5 patients dropping out due to mask intolerance. No significant improvements were found in daytime pulmonary function or blood gas values, treadmill walking time, symptom scores, or sleep quality. Neuropsychological

testing revealed a minimal improvement that was unexplained physiologically. Subsequently, Meecham-Jones et al[46] reported a trial of almost identical design on 18 patients who had improvements in daytime blood gas values, indicators of quality of life, and total sleep time, after 3 months of BiPAP ventilation. Patients in the Meecham-Jones study had substantially higher initial arterial CO_2 tension (57 vs 47 torr) despite having less airway obstruction (FEV_1 801 vs 560 mL). In addition, patients in the Meecham-Jones study had progressive nocturnal CO_2 retention and oxyhemoglobin desaturation that was not seen in the Strumpf study. This raises the possibility that COPD patients with severe CO_2 retention (> 55 torr) and sleep disordered breathing may constitute a subgroup apt to respond to NPPV.

As yet, however, 2 subsequent controlled studies have failed to confirm this possibility. Gay et al[47] screened 85 patients with severe CO_2 retention and eliminated all but 13 because they declined entry, had concomitant severe illness, or spontaneously improved during a pre-entry observation period. The 13 were randomized to receive NPPV or standard therapy for 3 months. Only 4 of the 7 randomized to receive NPPV (mean P_{aCO_2}, 55 torr) completed the trial, and no significant improvement was detected in these patients. More recently, Lin[48] performed an in-patient crossover trial on severe COPD patients with marked CO_2 retention (mean P_{aCO_2} 51 torr). He found no improvements in daytime gas exchange, functional status, or symptom scores after a 2-week period of NPPV compared to supplemental oxygen alone. Conclusions are limited by the small number of patients and, in the latter study, the brief duration of NPPV that was likely too short for adequate adaptation.

In Summary

Some evidence suggests that patients with severe CO_2 retention and nocturnal oxyhemoglobin desaturation may respond favorably to nocturnal nasal NPPV, and a trial may be warranted in such patients. On the other hand, the reported improvements are minimal and acceptance of NPPV by COPD patients has generally been poor, in contrast to that of patients with neuromuscular disease. At best, it appears that a relatively small minority of COPD patients may stand to benefit from NPPV. Well-designed trials on larger patient populations are clearly needed.

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The Prevention of Ventilatory Failure due to Inadequate Pump Function

John R Bach MD

Introduction
Patient & Problem Definition
The Respiratory Muscle Aids
Aids that Act on the Body
Aids that Act on the Airway
Glossopharyngeal Breathing
Patient Evaluation
Indications for Noninvasive Ventilation
Nocturnal Nasal NPPV & Survival
Prevention of Respiratory Failure
Future Research
In Summary

Introduction

The delivery of positive pressure ventilation (PPV) via nasal and oral-nasal interfaces (ie, noninvasive positive pressure ventilation, or NPPV) is now being widely explored as a means to eliminate the need to intubate patients in acute respiratory failure. However, it may be inadequate when patients are in respiratory failure due to severe lung disease. Such patients often have concomitant medical conditions and complicated courses and require supplemental oxygen. It has been suggested that supplemental oxygen and medications that depress hypoxic and hypercapnic ventilatory drive may decrease the effectiveness of the use of open systems like nasal NPPV during sleep.[1] The circumstances under which NPPV is cost-effective in allaying acute respiratory failure in the critical care unit remain to be seen. On the other hand, nasal NPPV was not used initially to treat patients with primary lung disease but rather as ventilatory assistance for patients with ventilatory pump failure.[2] In this paper, I consider the use of NPPV and other inspiratory and expiratory muscle aids to prevent pulmonary complications and respiratory failure in patients with inspiratory and expiratory muscle dysfunction. In my experience, many such patients have gone on to require 24-hour ventilatory support without ever being hospitalized or undergoing tracheostomy.

Patient & Problem Definition

The hypoxemia of patients with neuromuscular conditions and uncomplicated ventilatory insufficiency arising from respiratory muscle dysfunction can be corrected sufficiently to normalize oxyhemoglobin saturation without resort to supplemental oxygen. The most common diagnoses of patients amenable to this approach are provided in Table 1. Although patients with uncomplicated inspiratory and expiratory muscle failure can be managed using noninvasive respiratory muscle aids alone, this is not necessarily the case for patients with intrinsic lung disease nor for patients with severe bulbar muscle weakness who can have chronic aspiration of upper airway secretions and whose oxyhemoglobin saturation levels

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may not be normalized without supplemental oxygen. Only patients with uncomplicated respiratory muscle failure are considered here.

Table 1. Common Neuromusculoskeletal Conditions with Functional Bulbar Musculature, Leading to Ventilatory Failure

Myopathies—all generalized myopathies including the muscular dystrophies
Neurologic Disorders
Motor neuron diseases including spinal muscular atrophy types 2 and 3, motor neuron diseases, and poliomyelitis
Generalized neuropathies and phrenic neuropathies
Guillain-Barre syndrome
Multiple sclerosis
Disorders of supraspinal tone such as Friedreich's ataxia
Myelopathies of any etiology
Tetraplegia associated with pancuronium bromide anesthesia
Sleep-Disordered Breathing
Obesity hypoventilation
Central and congenital hypoventilation syndromes
Familial dysautonomia
Skeletal Pathology
Kyphoscoliosis
Osteogenesis imperfecta

Unless they are benefiting from the use of respiratory muscle aids, patients with neuromuscular conditions characterized by progressive muscle weakening inevitably develop acute respiratory failure. In my experience, this usually occurs during intercurrent upper respiratory tract infections (unpublished data) and results in hospitalization, intubation, mechanical ventilation and—after ventilator weaning fails—in tracheotomy. I have found this process usually to involve about 2 months of intensive care.

Although many centers have been making attempts to noninvasively maintain ventilatory function in the acute care setting, difficulties in clearing airway secretions appear to be the main reason for acute respiratory failure, for pneumonia, and, ultimately, for failure to wean from the ventilator. Despite the fact that the expiratory muscles have been reported to be weaker than the inspiratory muscles in many neuromuscular conditions,[3-11] and their function is critical for airway secretion clearance, I have observed few attempts to assist their function. I have found that although cough can usually not be assisted for patients with lung and airways diseases who usually have functional expiratory muscles, cough can be assisted and peak cough flows (PCF) greatly increased for patients with normal lung and airway tissues who suffer from neuromuscular conditions. I have demonstrated[12] that the ability to generate PCF > 180 L/min is the most important factor in permitting the 24-hour long-term use of NPPV as an alternative to ventilation via tracheostomy for patients with amyotrophic lateral sclerosis;[12] and, independent of any ability to breathe, the ability to generate PCF > 160 L/min can predict successful tracheal extubation and tracheostomy tube decannulation and transition to NPPV as necessary.[13] Thus, the ability to assist the expiratory muscles to increase cough flows can be, at least, as important as assisting the inspiratory muscles to maintain alveolar ventilation.

The Respiratory Muscle Aids

The respiratory muscles can be aided by manually or mechanically applying forces to the body or intermittent pressure changes to the airway.

Aids that Act on the Body

Body ventilators, including negative pressure body ventilators, act on the body. We have reported[14,15] on their use during tracheostomy-site closure for patients' being decannulated and switched to NPPV for ventilatory support. In addition, they can be useful temporarily to support patients with nasal congestion during upper respiratory tract infections and can also support small children with ventilatory muscle failure due to spinal muscular atrophy and other severe infantile neuromuscular diseases. However, we[16] have found them to be less versatile and generally less effective than NPPV, and we do not consider them practical for daytime aid. Because we[17] have found their use to be associated with frequent oxyhemoglobin desaturations due to obstructive sleep apneas, I will not discuss body ventilators further and refer the reader to another source.[18]

Intermittent abdominal pressure ventilator (IAPV) use can be practical for daytime ventilatory support. It consists of an air sac located in an abdominal binder. The sac is intermittently inflated by a positive pressure ventilator. This compresses the abdominal contents and moves the diaphragm, causing a forced exsufflation. During passive sac deflation, the abdominal contents and diaphragm fall to the resting position and inspiration occurs passively. Because effectiveness of the device depends on gravity, the user must sit at a trunk angle $\geq 30°$ from the horizontal. If the patient has any inspiratory capacity or is capable of glossopharyngeal breathing (GPB), he or she can add autonomous tidal volumes to the mechanically assisted inspirations. The IAPV generally augments tidal volumes by about 300 mL, but we have measured volumes as high as 1,200 mL.[19] Patients with < 1 hour of ventilator-free breathing ability often prefer using the IAPV while in a wheelchair rather than using NPPV.[19] The IAPV may be ineffective in the presence of severe scoliosis or obesity, but it continues to be an important body ventilator because it optimizes appearance and convenience.

A normal cough must be preceded by inspiration or insufflation to about 85-90% of total lung capacity[20] followed by the development of thoracoabdominal pressures sufficient to generate PCF > 6 L/s.[21,22] Total expiratory volume during normal coughing is about 2.3 ± 0.5 L.[20] PCFs decrease and may be inadequate to eliminate airway secretions as respiratory

muscles weaken. When the expiratory muscles are weak, they can be assisted with thrusts to the body by the caregiver. Nine methods of manually assisted coughing have been described.[23] For patients whose vital capacities (VCs) are below 1,500 mL, it is important first to provide a maximal insufflation before applying the abdominal thrust.[24] The goal is to approach normal cough volumes in patients with low VCs.

Manually assisted coughing has been demonstrated to significantly increase PCF for ventilator users with weak expiratory muscles. We have found that flows > 180 L/min can almost always be attained unless bulbar musculature is severely impaired. I believe that a patient with ventilatory pump failure whose bulbar muscle dysfunction is not so severe as to require an indwelling gastrostomy tube for nutritional support does not require a tracheostomy tube for ventilatory support irrespective of the extent of ventilatory muscle dysfunction. The effective use of manually assisted coughing, therefore, is essential for permitting long-term ventilatory support by noninvasive methods.

Aids that Act Directly on the Airway

NPPV can be provided even for 24-hour long-term ventilatory support. Air is delivered through the mouth (Fig. 1),[25-28] nose (Fig. 2),[29,30] or mouth and nose,[31-33] via appropriate patient-ventilator interfaces. I have found that patients almost invariably prefer the noninvasive approach to mechanical ventilation over ventilation via tracheostomy, for appearance, convenience, comfort, and security, and for facilitation of speech, swallowing, and sleep.[34] In my experience, the use of NPPV can reduce the cost of home mechanical ventilation by eliminating the hospitalizations, pneumonias, and other complications associated with tracheostomy PPV[35] and by reducing the costs associated with airway suctioning and tracheostomy-site care, including the need for nursing services.[36]

Although IAPV and GPB can also be used for daytime ventilatory support, mouthpiece NPPV is widely used and is, I believe, the most important method of noninvasive daytime ventilatory support because it permits the user to vary volumes easily while optimizing convenience and appearance.[34] The air is usually delivered to the patient via a simple mouthpiece affixed to motorized wheelchair controls. A telephone holder or a flexible metal gooseneck clamp allows easy access by minimal neck rotation and flexion. Some patients prefer to keep a small flexed mouthpiece in the mouth except when eating. My group[25] has reported on a series of 257 ventilator users who have used up to and including 24-hour mouthpiece NPPV as an alternative to tracheostomy PPV for a mean of 13.2 ±12.2 years.

'Air stacking' involves taking consecutive ventilator-delivered volumes without exhaling. Patients initially are taught air stacking as 'range-of-motion' therapy for the lungs and chest wall, to maximize the insufflation capacity, to maintain pulmonary compliance, and to prevent atelectasis. The goal

Fig. 1. A 72-year-old high-level acute traumatic tetraplegic woman who was intubated upon hospital admission. She was extubated after 5 days of continuous positive pressure ventilation (PPV) despite having no ventilator-free breathing ability and vital capacity < 240 mL. She was placed on continuous mouthpiece PPV. Although she was warned to use lipseal retention for nocturnal ventilatory support, she maintained adequate ventilatory support during sleep by using a simple mouthpiece. After 1 month she weaned to nocturnal only aid, which she continued for 2 years.

Fig. 2. A 25-year-old man with Duchenne muscular dystrophy and severe scoliosis who, because of lip weakness too severe to allow him to use a mouth piece, used 24-hour nasal PPV for > 5 years. He used acrylic low-profile transparent nasal interfaces fabricated from plaster moulages.[31]

is to approach the predicted inspiratory capacity. The maximum volume of air that can be held is the maximum insufflation capacity (MIC). Air stacking can temporarily improve dynamic pulmonary compliance and may help maintain static lung compliance.[37] The higher volumes increase both unassisted and assisted PCF and permit the patient to raise voice volume as needed. Demonstration of the patient's ability to air stack lets the clinician know that the patient is capable of mouthpiece and nasal NPPV should acute ventilatory failure develop. In my experience,[18] intubated patients with no ventilator-free breathing ability but whose oxyhemoglobin saturation is essentially normal without supplemental oxygen and who have learned to air stack can be safely extubated and switched directly to NPPV.

Patients whose neck or lips are too weak to grab a mouthpiece usually prefer to use an IAPV or nasal interface for NPPV for daytime aid rather than to undergo tracheotomy. Nasal NPPV is now also the most popular method of nocturnal ventilatory support. In 1981,[2] as an alternative to mouthpiece NPPV for French muscular dystrophy patients, NPPV was delivered via nasal interfaces consisting of 2 Foley catheters. My group[29,38] subsequently described nasal NPPV for use during sleep by patients with little or no measurable VC or ventilator-free breathing ability. Commercially available continuous positive airway pressure (CPAP) masks became available for the treatment of sleep disordered breathing in 1984 and were soon also used to deliver nasal NPPV. Because these interfaces are not always comfortable or leak free during nasal NPPV, custom-molded varieties have been developed.[31] With the many CPAP masks now on the market, however, it is becoming increasingly uncommon to need to resort to the fabrication of custom interfaces. The attributes of NPPV interfaces are summarized in the Appendix.

Strap-retained oral-nasal interfaces have been available for use during anesthesia, and a new strap-retained oral-nasal interface is now available for long-term nocturnal ventilatory support (Respironics Inc, Murrysville PA). Strapless oral-nasal interfaces were described in 1989.[32] These interfaces not only provide an essentially airtight seal for the delivery of PPV, but also a simple tongue thrust is all that is necessary to expel them. The bite-plate retention is also important for ventilator users living alone who are unable to don straps because of inadequate upper extremity function.[33]

Mechanical insufflation-exsufflation acts directly on the airway to assist or substitute for expiratory muscle function in the elimination of airway secretions. An In-Exsufflator (JH Emerson Co, Cambridge MA) provides an insufflation that can be delivered via any upper airway interface, most often, an oral-nasal interface or an indwelling translaryngeal or tracheostomy tube. This is followed by a forced exsufflation that serves as an expiratory aid. Insufflation and exsufflation pressures are independently adjusted for comfort and effectiveness in the range of +30 to +50 cm H_2O and −30 to −50 cm H_2O. The insufflation takes place over 2-3 seconds. The pressure change to exsufflation occurs in about 0.02 seconds and is usually sustained for several seconds. An abdominal thrust should be timed to the exsufflation cycle, especially when mechanical insufflation-exsufflation is used through the upper airway. Cycling between positive and negative pressure can be done manually or automatically, depending on the model being used. The manual cycling feature facilitates caregiver-patient coordination of inspiration and expiration with insufflation and exsufflation but requires a third hand when one wants to deliver a concomitant abdominal thrust or if an additional hand is needed to secure the mask. With our patients, a treatment consists of about 5 cycles of insufflation-exsufflation followed by a period of normal breathing or ventilator use for 20 to 30 seconds to avoid hyperventilation. The treatments continue until no further secretions are expelled and can be repeated every 5-10 minutes as needed.

I have found that decreased VC, pulmonary flow, and oxyhemoglobin saturation return to baseline levels when mucus plugs are cleared.[24] An early study[39] reported marked increases in VC for patients with bronchiectasis, asthma, and pulmonary emphysema. An increase in VC of 15-42% was also noted immediately following treatment in 67 patients with "obstructive dyspnea" and a 55% increase in VC was noted following mechanical insufflation-exsufflation in congested patients with neuromuscular conditions.[40] I have observed 15-300% improvement in VC and normalization of oxyhemoglobin saturation for acutely ill neuromuscular ventilator users.[24] An early study[41] demonstrated the device's efficacy when it was applied by oral-nasal mask to animals. I have observed that mechanical insufflation-exsufflation applied via an endotracheal or tracheostomy tube eliminates secretions without the airway irritation and discomfort caused by tracheal suctioning, and patients invariably prefer it to tracheal suctioning.

In our practice, mechanical insufflation-exsufflation has permitted us to extubate neuromuscular patients following general anesthesia, despite their having little or no ventilator-free breathing ability and to convert them to NPPV. It also permits us to avoid intubation or quickly to extubate neuromuscular patients with profuse airway secretions in acute respiratory failure during intercurrent respiratory tract infections. It can be an important part of an outpatient protocol to prevent pulmonary complications and respiratory failure.

Except for intercostal muscle strain in patients who have not been receiving regular deep insufflations and for whom insufflation pressures are increased suddenly, no complications have been reported with the use of mechanical insufflation-exsufflation. Colebatch in an early paper[42] noted that because the negative pressure applied to the airways is analogous to positive pressure on the surface of the lungs during a normal cough, it is improbable that this negative pressure can be more detrimental to the lungs than normal cough pressure. Bickerman[41] found no evidence of parenchymal damage, hemorrhage, alveolar tears, or emphysematous blebs in

the lungs of animals treated with insufflation-exsufflation. Barach and Beck[40] reported no serious complications in the 103 patients they treated with more than 2,000 courses of mechanical insufflation-exsufflation. No reports of damaging side effects have been disclosed in more than 6,000 treatments in over 400 patients, most of whom had intrinsic lung disease.[42,43] Consistent with this is the fact that in over 650 patient-years and hundreds of applications by our ventilator users with neuromuscular dysfunction, no episodes of pneumothorax, regurgitation of gastric contents, or pulmonary complications have been observed (unpublished data). Caution must be observed for bradycardias, and insufflation and exsufflation pressures should be increased gradually when mechanical insufflation-exsufflation is used for acute traumatic tetraplegics. Abdominal thrusts should not be applied to patients with full stomachs.

Parents of infants with spinal muscular atrophy type 1 often complain that their children are no longer sleeping more than 1 or 2 hours without awakening, startled and crying. This can be an indication of nocturnal hypoventilation. When such patients are treated with nasal NPPV, their sleeping can once again be undisturbed. These children may go on to require 24-hour ventilatory support, but parents often refuse tracheostomy tubes for these children. We have found simple, so-called bi-level positive airway pressure devices adequate for the ventilatory support of these small children. Patients with neuromuscular conditions characterized by central alveolar hypoventilation in the presence of VCs over 50% of predicted normal and adequate inspiratory pressures (eg, Ondine's curse, myotonic dystrophy, familial dysautonomia, myasthenia gravis, and certain generalized neuropathies) may also be adequately ventilated by such devices because they can spontaneously generate the necessary cough flows.

In our experience with adolescent and adult patients with most other neuromuscular conditions, the bi-level positive airway pressure devices are not powerful enough to provide optimal insufflations for assisted coughing or for attaining the maximum insufflation capacity (> 40 cm H_2O) and should not be used. Further, those devices are neither practical nor safe for the ventilatory support of these patients when they require daytime as well as nocturnal PPV. A list of the advantages and disadvantages of pressure- and volume-cycled ventilators is noted in Table 2.

Table 2. Pressure-Cycled versus Volume-Cycled Ventilators

Advantages of Portable Volume Ventilators
Can deliver higher volumes and at potentially higher pressures as needed for patients with poor lung compliance.
Flows can be adjusted for comfort.
Consume only 1/3 to 1/8 the electricity for comparable air delivery, permitting greater patient mobility for the same battery capacity.
Quieter
Lower mean thoracic pressure for the same peak airway pressure hampers cardiac preload less (particularly advantageous for patients with cardiomyopathies).
Permit air stacking to obtain maximum insufflations, to increase dynamic pulmonary compliance, to raise voice volume, and to increase cough flows.
Can be used to operate intermittent abdominal pressure ventilators.
Have alarms that can increase safety and facilitate effective use of nocturnal ventilation.
Disadvantages of Volume Ventilators
Heavy weight
Alarms can be annoying.
Needlessly complicated; ventilators with fewer modes should be available.
Advantages of Pressure-Cycled Ventilators
No annoying alarms
Lightweight
Less expensive
Can compensate to some extent for small insufflation leaks.
Disadvantages of Pressure-Cycled Ventilators
Not all can provide optimal volumes needed for coughing and maintaining lung compliance.
Do not allow air stacking.
Fixed, high initial flows on currently available machines can cause mouth drying and gagging (especially with leakage) and arousals from sleep.
High power consumption limits patient mobility.
Discomfort and increased thoracic pressures from unnecessary expiratory positive airway pressure
Peak pressure indication is less useful for feedback than with volume ventilator.
Absence of alarms decreases safety for some patients.
May be noisier than volume ventilators
Mean intrathoracic pressure is higher than with the volume-cycled ventilators.
Clinically important CO_2 rebreathing can occur in patients with expiratory positive airway pressures < 5 cm H_2O (can be corrected with nonrebreathing valve, at cost of greater expiratory resistance).
Expiratory positive airway pressure can make eating difficult or hazardous for 24-hour users.

Glossopharyngeal Breathing

Both inspiratory and, indirectly, expiratory muscle function can be assisted by GPB. In fact, this technique was first described as an aid for coughing.[44,45] It involves using the glottis to capture boluses of air and 'gulping' those boluses into the lungs. The glottis closes with each gulp. One breath usually consists of 6-9 gulps of 60 to 200 mL each. During the training period, the efficiency of GPB is monitored by spirometrically measuring the volume (mL) of air/gulp, gulps/breath, and breaths/minute. An old but excellent training film is now available on videotape (Rancho de los Amigos, 7601 E Imperial Way, Downey CA 90242).[45]

GPB can provide patients who have weak inspiratory muscles and no measurable VC or ventilator-free breathing ability with normal alveolar ventilation for hours and in perfect safety when they are not using a ventilator or in the event of sudden ventilator failure day or night.[46]

GPB can be effective for all patients except those with severe bulbar muscle weakness. More than 60% of patients with intact glottic function can master the procedure,[14,47] and it can even be effective for patients with Duchenne muscular dystrophy who have relatively severe bulbar muscle weakness.[48] Although potentially extremely useful, GPB appears to be taught rarely—perhaps because few health care professionals are familiar with the technique. GPB is rarely useful in the presence of an indwelling tracheostomy tube. It cannot be used when the tube is uncapped as it is during PPV via the tube. Even when the tube is capped, the gulped air tends to leak around the outer walls of the tube and out the tracheostomy site as airway volumes and pressures increase during the air stacking process of GPB. I believe that the safety and versatility afforded by effective GPB are key reasons to eliminate tracheostomy in favor of noninvasive aids.

Patient Evaluation

We screen patients for symptoms of chronic alveolar hypoventilation[29] and monitor VC, assisted and unassisted PCF, end-tidal carbon dioxide tensions, and oxyhemoglobin saturation determined by pulse oximetry (S_{pO_2}). The VC is measured with the patient both sitting and supine. The patient should also cough as hard as possible through a mouthpiece or, if the lips are too weak to grab the mouthpiece, through an oral-nasal interface, into a peak flow meter to measure the unassisted PCF. Patients with VCs < 1,500 mL[24] are insufflated via a manual resuscitator to maximal volumes, then an abdominal thrust is coordinated with glottic opening and the resulting assisted PCFs are read from a peak flow meter.[24] Patients with severely diminished VCs when supine (generally about 600 mL for Duchenne muscular dystrophy patients and 1,000 mL for most others) or daytime hypercapnia or S_{pO_2} < 95% undergo nocturnal S_{pO_2} monitoring.

Arterial blood gas monitoring and polysomnography are rarely useful for these patients. Although some clinicians are advocating the use of polysomnography to detect early evidence of sleep-disordered breathing to introduce nocturnal nasal NPPV, it has not been demonstrated that patients with neuromuscular conditions who are as yet asymptomatic for sleep hypoventilation and who have mean nocturnal oxygen saturations ≥ 94% benefit from nocturnal nasal NPPV. Symptomatic hypoventilation in these patients is due primarily to inspiratory muscle weakness and not to central or obstructive apneas. I believe that the appropriate treatment is NPPV, not CPAP or supplemental oxygen. On the other hand, polysomnography is warranted for symptomatic patients with adequate supine VC (> 50% of predicted) who may have predominantly central or obstructive sleep apneas without severe concomitant inspiratory muscle weakness. These patients can have any primary diagnosis and be diagnostic puzzles. I believe that central alveolar hypoventilation is too common in patients with myotonic dystrophy, familial dysautonomia, morbid obesity, and Ondine's curse to warrant polysomnography. It can usually be adequately documented by simple oximetry and noninvasive monitoring of blood carbon dioxide tensions.

Indications for Noninvasive Ventilation

The speed of progression of illness, VC in the supine position < 40% of predicted normal, the extent of hypercapnia, the mean nocturnal oxyhemoglobin saturation, and the presence of symptoms of alveolar hypoventilation are all considered in prescribing NPPV. The presence of obvious symptoms of chronic alveolar hypoventilation or hypercapnia and mean nocturnal S_{pO_2} < 94% are indications to introduce nocturnal NPPV by nasal interface or mouthpiece with lipseal retention (Fig. 3) as preferred by the patient. In general, our patients are encouraged to use nocturnal NPPV if it makes them feel better and improves their nocturnal mean S_{pO_2}.

Fig. 3. A high-level acute tetraplegic man using mouthpiece PPV with lipseal following tracheal decannulation.

Although nightly ventilatory assistance can be instituted for the listed clinical indications, the majority of patients remain stable, often despite varying degrees of chronic hypercapnia and subtle symptoms, until an otherwise benign upper respiratory tract infection causes airway secretions that the patient cannot effectively clear (unpublished data). As previously noted, this may result in a long stay in intensive care and, ultimately, tracheostomy. We have found that patients with VCs > 1,500 mL and unassisted or assisted PCF > 270 L/min have little risk of developing acute respiratory failure during periods of airway hypersecretion. Patients with paralytic-restrictive pulmonary syndromes who satisfy the indications for introduction of nocturnal NPPV or who may not quite satisfy these criteria but who have maximum unassisted or assisted PCF < 270 L/min are considered to be at risk of developing airway-secretion-associated acute respiratory failure and are placed on a preventive treatment protocol to main-

tain normal alveolar ventilation and adequate PCF during periods of need. Patients with severe bulbar muscle dysfunction whose assisted PCF cannot exceed 160 L/min may also use this protocol, but it is likely to fail. Such patients require invasive methods because of inability to eliminate airway secretions due to airway instability. Typical patients in this category are those with bulbar amyotrophic lateral sclerosis and spinal muscular atrophy type 1.

Nocturnal Nasal NPPV & Survival

I recently reviewed 20 studies of nocturnal nasal NPPV that, in general, reported modest increases in tracheostomy-free survival for patients with paralytic/restrictive conditions.[35] Volume-cycled ventilators were used in 15 of the studies and pressure-cycled machines in the other 5. Except in our center, however, none of the previous studies reported the use of daytime NPPV or assisted coughing. A 1994 study[49] described some commonly held misconceptions concerning nasal ventilation. That study purported mortality to be increased by nocturnal use of nasal NPPV. Unfortunately, it was a 17-center trial in which only 35 subjects and controls were recruited, and there was no standardization in ventilator use, nasal interface use, caregiver or patient training, or follow-up. The authors stated that 15 of the 35 subjects did not use nasal ventilation the minimum 6 hours per night, and for the 20 subjects that they felt were "effectively ventilated," the conclusion was drawn from the history only. Nocturnal S_{pO_2} and carbon dioxide tensions were not monitored to demonstrate efficacy. The subjects were offered only one style of nasal interface. No effort was made to determine whether the interfaces were comfortable or were worn snugly. Because the patients were not offered daytime NPPV, assisted coughing, or nocturnal lipseal NPPV when nasally congested, it is not surprising that the authors found that the predominant cause of death was "mucus plugging during respiratory tract infections." Thus, this particular publication perpetrates many of the common misconceptions about NPPV: (1) nasal intermittent positive pressure ventilation is essentially the only method of NPPV, thus ignoring mouthpiece, lipseal, and oral-nasal interface use; (2) when nocturnal use of nasal ventilation is no longer adequate tracheostomy is required; (3) simple prescription of nasal ventilation can be enough without the participation of trained therapists to evaluate trials of various masks and to train in assisted coughing and oximetry feedback; and (4) the primary difficulty in preventing mortality in Duchenne muscular dystrophy and other patients with severe generalized weakness is in assisting ventilation rather than in effective evacuation of airway secretions.

Prevention of Respiratory Failure

I believe that ventilatory failure and the pulmonary infiltrates that often lead to acute respiratory failure can be prevented by instructing the patient in the home how to avoid alveolar hypoventilation and how to effectively eliminate airway secretions. Once the criteria are met for risk of respiratory failure due to airway secretions, the patient is equipped with an oximeter. He or she is instructed to use it whenever short of breath or severely fatigued, and to use it continuously during upper respiratory tract infections and other episodes characterized by production of excessive airway secretions. Many patients are already capable of using mouthpiece and nasal PPV because they have received a manual resuscitator for daily air stacking to maintain lung and chest wall elasticity. If they do not have this skill, they are now taught how to receive air via various mouthpieces and nasal interfaces. They choose the ones that are most comfortable and allow the best seal. They are also given a lipseal for use when nasally congested. All patients are also taught manually assisted coughing, and they try mechanical insufflation-exsufflation in the clinic (Fig. 4).

Fig. 4. A 72-year-old acute high-level tetraplegic whose tracheostomy tube was removed despite his having a vital capacity of only 120 mL and no ventilator-free breathing ability. He required mechanical insufflation-exsufflation in the acute setting and daily thereafter because of frequent food aspiration. He remained dependent on 24-hour NPPV.

The clinician must be satisfied that the patient has mastered all of the major methods of inspiratory and expiratory muscle assistance. The patient and care providers are instructed to always maintain $S_{pO_2} > 94\%$, particularly during respiratory tract infections. At the first sign of illness, the patient who is not already equipped is sent a portable volume ventilator and a mechanical insufflator-exsufflator. The patient is told that a decrease in S_{pO_2} below 95% is considered evidence of hypoventilation or acute bronchial mucus plugging. During upper respiratory tract infections patients usually require continuous use of NPPV, both for ventilatory support and for air stacking for manually assisted coughing. There-

fore, desaturations, particularly sudden ones, are usually due to bronchial mucus plugging for which the patient uses manually and mechanically assisted coughing. Although it is not uncommon for the S_{pO_2} baseline to decrease to as low as 92% in febrile patients with respiratory tract infections, greater decreases in baseline S_{pO_2}, gross atelectasis, and pneumonia are uncommon in patients managed by this approach, in our experience. This is true despite the fact that many patients who do not otherwise require ventilator use, require 24-hour ventilatory support with no ventilator-free breathing ability during these episodes. It seems obvious that these patients would otherwise develop acute respiratory failure and be managed in critical care units if they were not benefiting from 24-hour ventilatory support and effective assisted coughing at home. Patients who already require nocturnal NPPV almost invariably require 24-hour NPPV during acute episodes. The patient is never provided with supplemental oxygen at home and cannot develop respiratory failure with a normal S_{pO_2}. The avoidance of supplemental oxygen and the maintenance of essentially normal oxyhemoglobin saturation are crucial. All patients are also supported with antibiotics and decongestants as warranted.

As the acute episode passes, previously autonomously breathing patients are often weaned to nocturnal NPPV or weaned off mechanical assistance entirely until the next episode. If treatment is delayed or the protocol fails and the S_{pO_2} baseline decreases to < 92% or if there are concurrent conditions such as apparent dehydration, the patient presents for further evaluation and possible hospitalization and conventional management.

As respiratory muscle weakness increases and oxyhemoglobin desaturations are due to hypoventilation during daytime hours, it is demonstrated to the patient that S_{pO_2} can be normalized either by volitionally taking deeper breaths or by receiving deep insufflations via a mouthpiece or nasal interface. The patient may then briefly use oximetry as a guide to the use of NPPV as necessary to improve ventilation during daytime hours. It is in this manner that we now have patients who have weakened to the point of requiring ongoing 24-hour ventilatory support without ever being hospitalized or intubated.

A summary of our pilot data includes:

- 45 patients with neuromuscular conditions who did not benefit from our approach and who underwent tracheotomy after hospital admission for acute respiratory failure spent a mean of 70.1 days in the hospital as compared to 4.1 days for patients introduced to NPPV.
- 40 patients who satisfied criteria for our protocol and were using up to 16 hours of daily NPPV and assisted coughing when necessary had 83 episodes that otherwise would have required hospitalization for ventilatory-respiratory failure in 165.1 patient years. However, they were hospitalized only 15 times for a mean of 3.1 days/patient and no patient required intubation. Patients requiring > 16 hours/day of NPPV had 32 episodes that otherwise would have required hospitalization in 95.9 patient years. There were, however, only 4 hospitalizations during this time for a total of 35 days or about 1 day for every 3 years of full-time noninvasive IPPV use (unpublished data).

Future Research

The mechanisms by which the open systems of NPPV can be effective during sleep require exploration. What roles do passive (as opposed to reflex) sealing of the oropharynx to NPPV insufflation leakage play? Future research also needs to better define the role of mechanical insufflation-exsufflation both in the management of patients with ventilatory impairment and for patients primarily with disease of the airways. Its efficacy when used via an endotracheal or tracheostomy tube should also be compared with that of invasive airway suctioning. Considering that patients with wounds of the abdomen or chest have reported less wound pain during mechanical insufflation-exsufflation than when coughing spontaneously,[50] should research in the role of mechanical insufflation-exsufflation be expanded? Finally, in the view of the efficacy and overall desirability of NPPV even full-time (as opposed to PPV by tracheostomy), research might be undertaken to determine the key reasons that noninvasive aids are not more widely used for patients with primarily ventilatory impairment.

In Summary

Mouthpiece NPPV is the most versatile and patient-preferred method of long-term daytime noninvasive ventilatory support.[25] Even patients who continue nasal NPPV into daytime hours on their own during acute episodes do not often find 24-hour nasal NPPV, that is, being connected to a ventilator by a nasal interface, to be an acceptable long-term solution. However, nasal NPPV is usually the patient-preferred method for nocturnal aid,[29] although mouthpiece NPPV with lipseal can be more effective, especially when the nostrils are sealed.[25] Patients almost invariably prefer NPPV over PPV via tracheostomy for appearance, convenience, comfort, and security and for facilitation of speech, swallowing, and sleep.[34] The use of NPPV decreases cost by decreasing hospitalization days, pulmonary complications, and the costs associated with maintaining an indwelling tracheostomy, including the use of disposable suction catheters and tracheostomy care.[36] Because of the need to attain maximal insufflations for assisted coughing, adolescent and adult patients with ventilatory muscle dysfunction should use portable volume-cycled rather than the pressure-cycled ventilators that are currently on the market because the latter cannot provide volumes of adequate depth for maximal lung insufflation. Finally, an approach using NPPV to maintain alveolar ventilation, assisted coughing to clear airway secretions, and oximetry for feedback can keep S_{pO_2}

within normal limits without resort to supplemental oxygen or tracheal intubation. This can decrease or eliminate hospitalizations for respiratory impairment for patients with primarily ventilatory dysfunction.

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APPENDIX—Interfaces for Noninvasive Positive Pressure Ventilation

Interface	Description	Advantages	Disadvantages	Sources
Mouthpiece	Plastic, attaches directly to ventilator tubing, can be held, kept in mouth, or attached to wheelchair controls.	Inexpensive, comfortable, commercially available, facilitates speech & eating	Long-term use can cause orthodontic deformity, occasional allergy to plastic; may interfere with mouthstick activities.	Ventilator accessory manufacturers
Bennett lipseal with mouthpiece	Plastic flange, fits over mouth & seals lips around mouthpiece, retained by straps or headgear; soft mouthpieces can also be accommodated.	Firmly establishes the mouthpiece & decreases or eliminates leak during sleep. Systems pressures of 30-40 cm H_2O can be maintained.*	Interferes with speech; may increase secretions & likelihood of aspiration; secretion removal during infections may mandate removal; adequate seal may be difficult with bearded patients; possible allergy to plastic.	Nellcor Puritan Bennett, Boulder CO
Custom-molded mouthpiece	Plastic lipseal retained by bite plate; may have metal clasps.	Can be removed by tongue thrust; system pressure > 60 cm H_2O have been maintained.	Bite plate may stimulate excessive oral secretions or gag reflex; depends on adequate dentition; expensive	Department of Physical Medicine & Rehabilitation at NJ Medical School, Newark NJ
CPAP mask	Plastic nasal seal or pillows, retained by headgear or straps	Simple, inexpensive, durable, commercially available	Fitting by trial & error; seal may be inadequate at higher pressures.	CPAP & ventilator accessory manufacturers
Custom-molded nasal mask	Several varieties commercially available	Commercially available & comfortable	Fabrication difficult for some faces; heavy; replacement required in 2-5 months; relatively expensive.	SEFAM from LifeCare International, Westminster CO
Interface for Ventilator-Assisted Living (IVAL)	Custom molded, butterfly shape, covering nostrils & extending over cheeks; soft inner gasket with nasal opening	Comfortable, ≥ 2-year use; leak free for most patients	Must be made from facial impression in supine position for best fit; gasket must be replaced every 3-9 months.	Department of Physical Medicine & Rehabilitation at NJ Medical School, Newark NJ
Oral-nasal interfaces (ONI)	Modified anesthesia masks cover nose & mouth; soft, flexible inner lining creates seal as air enters interface.	May provide a better seal than nasal mask or simple mouthpiece, particularly for obtunded or critically ill patients.	Covers both nose & mouth; may increase risk of aspiration.	Respironics Inc, Murrysville PA
Custom-molded strapless ONI	Acrylic bite plate attached to acrylic extra-oral shell; allows simultaneous nasal & mouthpiece ventilation.	Can be removed by tongue thrust; speech not hampered; air tight.	Expensive; requires adequate dentition; may stimulate excessive oral secretions or gag reflex; may require frequent adjustment initially to eliminate leak & assure comfort.	Department of Physical Medicine & Rehabilitation at NJ Medical School, Newark NJ Department of Cardio-pulmonary Services, Dallas Rehabilitation Institute, Dallas TX

*For patients with sporadic, nocturnal nasal leakage, cotton pledgets may be sealed in the nose with tape.

Pediatric Application of Noninvasive Ventilation

W Gerald Teague MD

Introduction
Experience
- **Obstructive Sleep Apnea**
- **Nocturnal Obstructive Hypoventilation**
- **Central Hypoventilation**
- **Chronic Restrictive Lung Disease**
- **Chronic Obstructive Airways Disease**
- **Acute Hypoxemic Respiratory Failure**

Technology
- **Airway Interface**
- **Delivery Systems**
- **Supplemental Oxygen**
- **Airway Pressure Monitoring**
- **Maintenance**

Contraindications
Complications
Compliance
Treatment Criteria
- **Patient Selection**
- **Titration of Airway Pressures**
- **Patient Monitoring**

In Summary

Introduction

The term noninvasive positive pressure ventilation (NPPV) refers to a method of ventilatory assistance whereby the ventilator is interfaced with the patient via a nasal or face mask. As with other forms of assisted ventilation, the ultimate purpose of NPPV is to enhance alveolar ventilation. The challenge today is to identify those clinical situations in which NPPV may be superior to standard therapy in accomplishing that purpose. NPPV has been studied extensively in adults with several etiologies of respiratory disease and found generally to be effective.[1-4] NPPV appears to be an equally promising therapy in children, but published reports of its efficacy in pediatric-age patients are relatively few and limited to uncontrolled case series.[5] As a result, at this time (1997), there are no well-defined clinical settings in which NPPV can be considered as standard therapy in pediatrics. In this paper, I review the experience with NPPV in children with respiratory diseases to provide an overview of the various technical issues, contraindications, and treatment criteria relevant to its most effective application. The review does not cover other modes of assisted ventilation sometimes referred to as noninvasive, such as negative pressure ventilation, positive pressure abdominal breathing, or positive pressure ventilation via a mouthpiece.

Beginning in the late 1980s, the use of NPPV for assisted ventilation for children began to grow steadily. Three con-

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current trends in pediatric respiratory medicine are likely explanations. First, advances in respiratory care have improved survival in children with acute respiratory failure. Recovery from severe lung injury is often prolonged, and survivors can require ventilatory assistance for weeks to months.[6] NPPV has been used effectively in adult patients as a component of the weaning process.[7] Second, increased utilization of sleep polysomnography as a diagnostic tool has advanced both the identification and classification of nocturnal respiratory disturbances in pediatric patients. As one example, polysomnographic studies have shown that recurrent airway occlusions can result in hypoxemia and disrupt sleep in children with Duchenne muscular dystrophy.[8] Although controlled trials are lacking, these events may be reduced by nocturnal NPPV.[5] Third, soft nasal masks and flow-triggered devices to accomplish NPPV are readily available from private vendors. These devices are both portable and easy to use in the domestic setting. However, commercial availability of devices suitable for pediatric application of NPPV has outpaced the completion of controlled clinical trials confirming their efficacy.

Experience

Obstructive Sleep Apnea

The etiology, clinical manifestations, and treatment of obstructive sleep apnea (OSA) in children are different from those in adults.[9,10] Children with OSA may present with nocturnal respiratory dysfunction ranging from obstructive apnea with mild hypoxemia to prolonged episodes of obstructive hypopnea with hypercarbia.[11] In many cases, adenotonsillectomy cures OSA in children, but bridge therapies preceding surgery include either supplemental oxygen alone or continuous positive airway pressure (CPAP) administered via nasal mask.[10,12-15] Nasal CPAP is an effective therapy in children with OSA,[16] but its use in some patients can lead to central apnea and increased hypoventilation.[13] The phenomenon of CPAP-induced central hypoventilation has been described in obese adults with nocturnal OSA and hypercarbia, who subsequently were effectively treated with NPPV.[17]

In patients with OSA, episodes of airway occlusion often occur at end-expiration.[18] Such occlusions 'load' the inspiratory muscles, which must develop considerable force to open the airway during the subsequent inspiratory effort. Inspiratory muscle fatigue is thought to play an important role in the pathophysiology of OSA. Consequently, therapies to assist inspiratory effort might potentially improve patient comfort. Sanders and colleagues[19] successfully applied a flow-triggered inspiratory pressure assist unit to reduce apnea frequency and improve comfort in adults with OSA. This device was ultimately released for the treatment of OSA in adults (BiPAP® system, Respironics Corporation, Murrysville PA) and is used frequently today to accomplish NPPV due to its capacity to raise tidal volume through an adjustable inspiratory pressure assistance feature.[20]

At the present time, there is no clear consensus as to the role of NPPV in patients with OSA. In uncontrolled reports, NPPV with a bi-level positive pressure device did acutely improve respiratory gas exchange in children with OSA and was, in general, well tolerated.[21,22] Both CPAP and NPPV by nasal mask have been used to treat OSA in children who experienced respiratory decompensation following adenotonsillectomy.[23] However, further experience with NPPV in children with OSA is necessary to identify those patients who benefit.

Nocturnal Obstructive Hypoventilation

Nocturnal obstructive hypoventilation (NOH) is characterized by prolonged episodes of nocturnal obstructive hypopnea.[11] It may be diagnosed by polysomnography in infants and children with various causes for upper airway obstruction, including OSA, morbid obesity, Down syndrome, craniofacial anomalies, and congenital abnormalities of the larynx and trachea. Episodes of obstructive hypoventilation are characterized by partial airway narrowing accompanied by retractions and asynchronous movements of the thorax and abdomen. During the rapid eye movement (REM) sleep phase, NOH is most evident due to reduced tone in the muscles supporting respiratory function. NOH can result in alveolar hypoventilation when the airway obstruction is so severe that the respiratory muscles cannot compensate. Untreated NOH in children can lead to chronic respiratory failure and eventual death from pulmonary artery hypertension and cor pulmonale.[24]

Surgical procedures to improve the patency of the upper airway are indicated in children with NOH. In life-threatening cases, tracheotomy may be necessary. However, the surgical approach is often complex, such as that for craniofacial disorders, and is often staged over a prolonged period of time.[25] In an uncontrolled report, NPPV in a small sample of children with NOH acutely reduced the number of airway occlusions, lowered nocturnal CO_2 tension, and improved oxygenation.[21] This study sample included a child with obesity, restrictive lung dysfunction, and prolonged nocturnal hypopnea in whom nasal-mask CPAP treatment increased the severity of central apnea (Fig. 1). Treatment of this subject with NPPV acutely improved respiratory gas exchange and was accompanied by a reduction in inspiratory muscle effort (Fig. 2). However, these findings are preliminary and carefully controlled studies are indicated to examine whether NPPV can be safely used long term as a bridge to surgery in children with NOH.

Central Hypoventilation

Congenital central hypoventilation usually presents shortly after birth, with cyanosis and prolonged episodes of central apnea/hypopnea that are manifest during sleep. Infants with congenital central hypoventilation syndrome typically do not respond to respiratory stimulants and, therefore, typically undergo diaphragmatic pacing for long-term care. However,

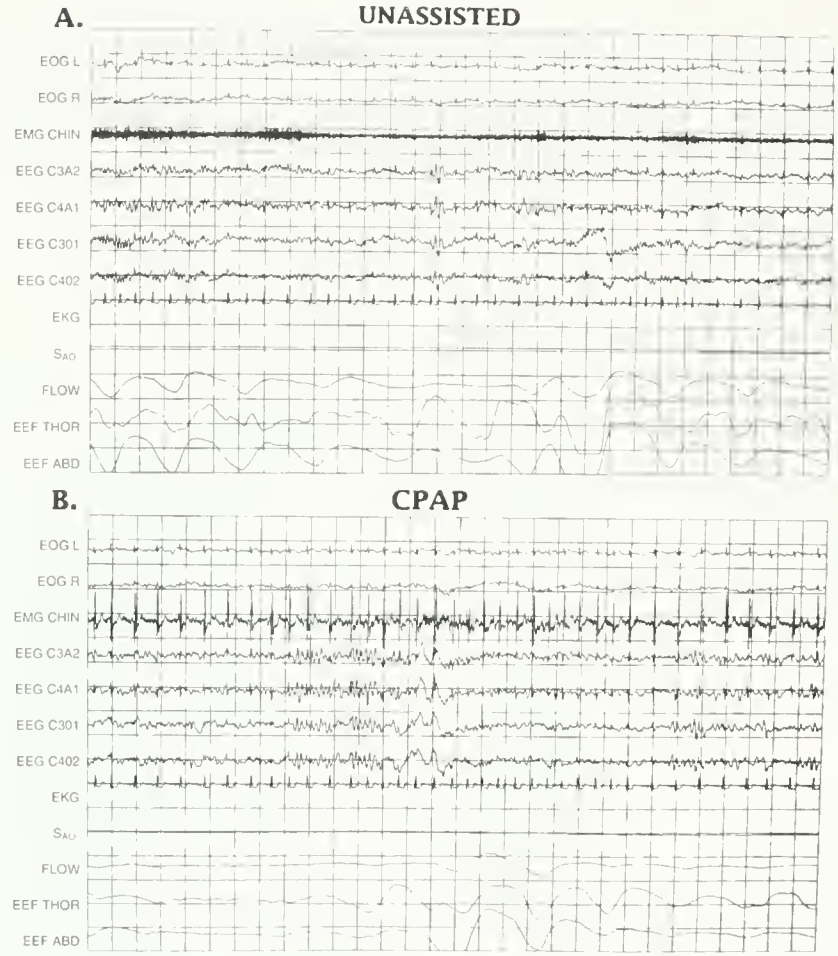

Fig. 1. Polysomnography results from a 15-year-old girl with Prader-Willi syndrome. A. Unassisted breathing with an episode of obstructive apnea (absence of air flow) preceded by asynchronous motion of the thorax (EEF THOR) and abdomen (EEF ABD). The oxyhemoglobin saturation by pulse oximetry (S_{pO_2}) fell to 83% and the carbon dioxide tension by transcutaneous monitor (P_{tcO_2}, labeled as S_{AO_2} on tracing) increased to 46 torr despite sustained respiratory effort. B. Nasal CPAP of 8 cm H_2O and F_{IO_2} of 0.30 started at 2 hours into the study led to prolonged episodes of central apnea (absence of air flow with no respiratory effort) and worsening of both the hypoxemia and hypercarbia. Each vertical line is 1 second. The P_{tcO_2} tracing is not shown. EOG L and R = left and right eye oculograms, EMG CHIN = chin electromyogram, EEG = electroencephalogram, EKG = electrocardiogram, EEF THOR = thoracic effort, EEF ABD = abdominal effort.

there are isolated case reports of successful NPPV in older children with central hypoventilation syndrome.[26,27] The use of NPPV for the treatment of infants with congenital central hypoventilation in place of standard therapies has not been studied and cannot be recommended at this time.

A role for nasal mask CPAP or NPPV in the treatment of children with central hypoventilation from other causes is also yet to be established. Conditions with a reduced central respiratory drive in which NPPV could be a useful therapy include myelomeningocele with the Arnold-Chiari malformation and idiopathic central apnea. In adults with central sleep apnea, CPAP therapy does reduce the frequency of central respiratory pauses,[28] but clinical trials in patients with Cheyne-Stokes respiration and congestive heart failure have shown both beneficial[29] and detrimental effects.[30]

Chronic Restrictive Lung Disease

Duchenne muscular dystrophy,[31-33] kyphoscoliosis,[34,35] and tuberculosis accompanied by restrictive lung dysfunction[36] are amenable to long-term nocturnal treatment with NPPV in adult patients. Although lung function in these patients does not improve significantly, daytime arterial CO_2 levels fall after a relatively brief trial of nocturnal NPPV.[37] In patients with chronic hypercarbic respiratory failure, lowering the P_{aCO_2} at night with NPPV may restore the central ventilatory response to hypercarbia. Both flow-triggered units and intermittent positive pressure ventilators may be used to accomplish NPPV in patients with restrictive dysfunction. In a short-term study, NPPV with devices providing either intermittent inspiratory positive pressure or inspiratory pressure assistance raised tidal volume and improved oxygenation better than CPAP in adults with stable chronic respiratory failure.[38]

Although published trials of NPPV in children with restrictive lung dysfunction are few in number and uncontrolled, the results are promising. Nasal-mask inspiratory pressure assistance improved sleep quality and reduced the number of hospital days in children with respiratory failure from neuromuscular weakness.[39] Further studies are indicated to examine whether nocturnal NPPV actually prolongs survival in children with these conditions, as it probably does in adult patients with Duchenne muscular dystrophy.[32]

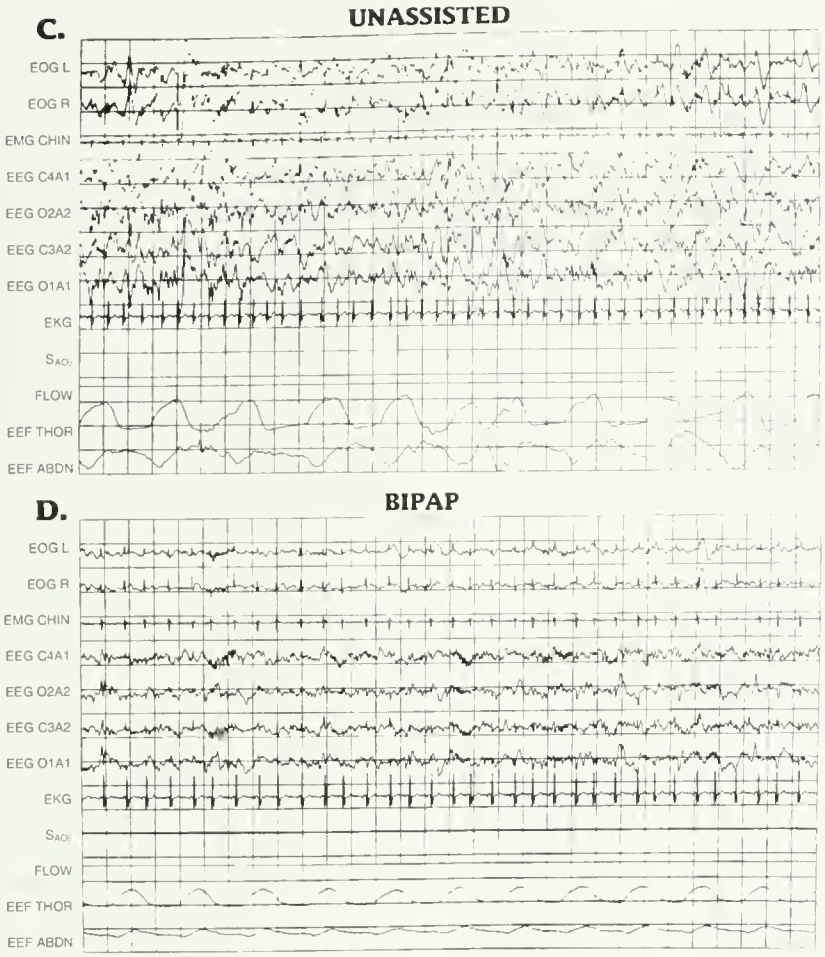

Fig. 2. Polysomnography results from the patient in Figure 1 performed 12 nights later. C. Baseline period of unassisted breathing with a prolonged episode of continuous thoraco/ abdominal asynchrony accompanied by a reduction in S_{pO_2} (ie, S_{AO_2}) to 89%. D. Effects of NPPV with the BiPAP device adjusted to 16 cm H_2O inspiratory pressure, 6 cm H_2O expiratory pressure, and F_{IO_2} of 0.21. Note the complete resolution of thoraco-abdominal asynchrony and reduction in thoracic effort. The S_{pO_2} increased to 94% and the P_{tcO_2} fell to 43 torr. The time scale and abbreviations are the same as in Figure 1. The S_{pO_2}, P_{tcO_2}, and flow tracings are not shown.

Chronic Obstructive Airways Disease

Respiratory muscle fatigue, often associated with inadequate nutrition, is an important contributing factor in the path to respiratory failure in patients with chronic obstructive airways disease (COAD). NPPV could be used to 'unload' the inspiratory muscles and, thereby, raise minute ventilation in those patients whose compensatory effort is limited by muscle fatigue. In one short-term study, NPPV but not mask CPAP reduced inspiratory muscle activity in adults with COAD.[38]

Clinical trials in adults with COAD show that NPPV is an effective treatment for exacerbations often triggered by respiratory infections accompanied by worsening hypercarbia. In adult COAD patients with acute decompensation, NPPV via full face mask reduced inspiratory muscle activity and avoided intubation.[40] This finding has been confirmed in other studies[41] and is the basis for the designation of NPPV as the treatment of choice to avoid intubation in this specific clinical setting.

The effects of long-term nocturnal NPPV in adult patients with COAD are by comparison to the acute experience less promising in regards to providing a clear benefit.[36,42] When outcome measures such as pulmonary function and respiratory gas exchange are examined, nocturnal NPPV has no clear advantages over standard therapy in this group of patients. However some benefits have been described, including improved sleep quality[43] and respiratory muscle rest.[44]

In children with cystic fibrosis, an uncontrolled trial of nocturnal NPPV was well tolerated and used as a bridge therapy to lung transplantation.[45] Similar to adults with COAD, NPPV may be a promising therapy in patients with cystic fibrosis admitted to the hospital with acute clinical exacerbations. Further studies are indicated to examine the role of NPPV in cystic fibrosis. Potentially ripe areas for exploration include the effects of nocturnal NPPV on growth variables, resting energy expenditure, and mucociliary clearance of secretions in cystic fibrosis patients.

There may be a role for portable flow-triggered devices in the home care of children with bronchopulmonary dysplasia (BPD) and tracheostomy. The rationale for such devices over conventional ventilators for home use is based on their portability and simplicity. However, the cumulative reported experience using this method is preliminary, and limited to 10 infants.[46] A technical issue that may limit the use of NPPV

in children with BPD is the limited peak inspiratory pressure capability of portable units (20 cm H_2O for the Respironics BiPAP system, 30 cm H_2O for the Healthdyne Quantum® unit). These peak pressures may not be adequate to overcome the high mechanical impedance to ventilation inherent in conditions in which airway resistance is great.[47] This limitation may be overcome with high performance ventilators, but experience with this method using a nasal mask interface in pediatric patients has not been widely reported.

Acute Hypoxemic Respiratory Failure

Numerous reports confirm the efficacy of NPPV in preventing intubation in adults with acute respiratory failure in the intensive care setting.[48-50] Experience with NPPV in pediatric-age patients with acute respiratory decompensation is also accumulating. NPPV acutely improved gas exchange in 2 critically ill toddlers with diffuse airspace disease in a case report.[51] In the intensive care unit of a children's hospital, NPPV with a BiPAP device improved oxygenation and avoided endotracheal intubation in a sample of children with acute hypoxemic respiratory failure.[52] The most common diagnosis in this case series was pneumonia, and a significant number of children with neurodevelopmental disabilities were managed effectively with this method.

Status asthmaticus can be accompanied by severe hypoxemia and respiratory muscle fatigue, that if not quickly reversed, lead to intubation. NPPV via face mask improved respiratory gas exchange in adult patients with severe hypoxemia from status asthmaticus,[53] but this study was not controlled. Routine use of NPPV in children with acute asthma at risk for respiratory failure is not recommended pending the outcome of controlled interventional studies.

Technology

Airway Interface

Soft preformed nasal masks are the usual interface between positive pressure device and the patient during pediatric application of NPPV. Masks suitable for NPPV are commercially available in a range of size and shapes. Some companies custom fit masks for children with unusual facial contours.[54] The nasal passages can also be sealed with prongs, typically used in small infants, or nasal pillows in older patients who do not tolerate the nasal mask.[55]

In adult patients with acute respiratory failure, full face masks have been used to administer NPPV as a means of avoiding intubation.[40] However, pediatric experience with full face masks is limited primarily to their use in administering CPAP to infants. Young patients are at considerable risk for aspiration as a result of immature airway protective responses. For this reason, NPPV via full face mask in infants and children should be considered a high-risk procedure, and attempted only in the intensive care unit setting with careful monitoring.

Delivery Systems

Several devices are available to accomplish NPPV in children, ranging from flow-triggered compact units to volume-regulated positive pressure ventilators. Each device has both advantages and disadvantages that are impacted by the age of the patient, the setting, and the pattern of respiratory dysfunction. Modern CPAP devices deliver positive pressure in increments of 2-20 cm H_2O via a bias flow profile ranging from 20 to 60 L/min. A bias flow is necessary to compensate for mask leaks and to maintain constant airway pressure during inspiration and expiration.[56] Rebreathing of expired gases is prevented by diverting expiratory flow through a non-rebreathing valve or by the leak of gas through small holes in the mask or fitting.

The Respironics BiPAP system is a portable flow-triggered device that allows independent adjustment of the inspiratory (IPAP) and expiratory (EPAP) airway pressures.[20] The resultant "bi-level airway pressure" profile has been effective in adults with OSA when the inspiratory pressure was higher than the expiratory pressure.[19] With appropriate adjustment of the inspiratory pressure, NPPV with this system can raise tidal volume and reduce inspiratory muscle activity in subjects with respiratory disease.[38] The Food & Drug Administration (FDA) recently approved it for use as a ventilatory-assist device.

Rebreathing of expired gases with the BiPAP is prevented by a one-way expiratory valve that is supplied with the unit. Whereas both inspiratory and expiratory gas flow is confined to a single circuit between the nasal mask and the unit, the level of end-expiratory pressure in the circuit is an important variable regulating the elimination of the patient's expired CO_2. In adult volunteers who underwent NPPV with the original exhalation valve supplied with the device, CO_2 rebreathing occurred when the EPAP level was < 5 cm H_2O. A new valve with improved CO_2 elimination characteristics is now available.[57]

Today, there are a number of flow-triggered portable units with performance characteristics suitable for NPPV in pediatric patients. Some of the more recently released devices offer an adjustable 'rise time' feature that can be used to control the rate of increase of the inspiratory pressure. This feature could affect patient tolerance of NPPV either positively or negatively, depending upon interdependent variables such as the spontaneous respiratory rate and the airway resistance. In a situation in which the airway resistance and respiratory rate are both high, a situation not uncommon in infants with respiratory distress, an overly long rise time might be inappropriate for the patient's ventilatory time constant.

Volume-cycled constant-flow generators have been reported to accomplish NPPV effectively in adults with respiratory dys-

function.[17,31,33,34,36,43,58-60] With few exceptions,[26] little has been published regarding this method in children. A constant tidal volume is adjusted, and the inflation pressure changes from breath to breath. Volume-cycled devices suitable for NPPV should be capable of delivering high inflation pressures and minute volumes because tidal volumes up to twice those used in intubated patients may be necessary to compensate for mask leaks and the increased dead space of the nasopharynx.[3] An automatic cycle feature is required in patients with weak inspiratory efforts or central apnea. An assist/control mode may be used to augment inspiratory efforts with machine-delivered inflations, but this mode may be impractical in infants and small children with some volume-cycled units. Piston-driven volume ventilators suitable for home use in pediatric patients should be modified by the addition of a supplemental flow source into the inspiratory circuit to accommodate spontaneous breaths.

Supplemental Oxygen

Supplemental oxygen is necessary to achieve normoxemia in patients whose oxyhemoglobin saturation remains < 90% after initiation of NPPV and can be added directly into the side port of the mask or the inspiratory circuit.[61] In practice, a relatively high flow of supplemental oxygen is required when the gas is blended into the circuit proximal to the venting valve because it is diluted by room air. However, an advantage of this method over introducing oxygen into a mask side port is that it facilitates precise measurement of the oxygen concentration by an analyzer located in the inspiratory tubing. In my experience, at least 5 L/min of 100% oxygen blended into the inspiratory line is necessary to raise the concentration above 25%. The inspired gas can be warmed and humidified by a humidifier with low compressible volume in the inspiratory circuit.

Airway Pressure Monitoring

The airway pressure(s) can be measured from the side port of the nasal mask by tubing configured in a T-circuit. One arm of the T leads to the positive pressure device and the other path to a standard manometer with an adjustable alarm feature. Standards for airway pressure monitoring with NPPV have not been adopted but are likely to be the standard of care when NPPV is used for life support or in those situations when an abrupt disconnect would be detrimental to the patient's safety. In the domestic setting, airway pressure monitoring with nasal CPAP is not routine[10] but should be considered in selected groups of at-risk patients with chronic respiratory failure treated with NPPV.

Maintenance

Manufacturers recommend cleaning the nasal mask with mild soap and water. Tubing can also be cleaned and air dried in the patients home. Conventional CPAP units and some ventilators have removable air filters that require periodic cleaning and replacement at regular intervals. Many manufacturers of positive pressure devices recommend annual maintenance of the unit, which consists of checking the integrity of the circuit, cleaning, and routine service. In the hospital setting, this function is typically performed by the departments of respiratory care and/or biomedical engineering. With domestic use, maintenance of the unit is the responsibility of the home care company.

Contraindications

Absolute contraindications to NPPV are uncommon in children. Choanal stenosis/atresia with clinically important obstruction of the nasopharyngeal airway precludes NPPV. Severe laryngomalacia is a relative contraindication in so far as positive pharyngeal luminal pressure may force the floppy epiglottis into the laryngeal inlet. However, infants with mild laryngomalacia, often associated with lower respiratory tract dysfunction, can benefit from NPPV. Excessive secretions may be a problem in children with depressed sensorium or impaired bulbar function and are a relative contraindication in settings in which they cannot be monitored and evacuated consistently. It may be impossible to achieve a secure mask fit in children with unusual facial anatomy. However, this too is a relative contraindication because many devices can compensate for mask leaks. I have applied NPPV with the BiPAP system effectively as a bridge to surgery in children with craniofacial anomalies.[25]

Respiratory clinicians are often reluctant to offer NPPV to children with respiratory distress due to the misconception that it will not be tolerated. NPPV-induced agitation is most likely to occur in children between the ages of 3 and 6 years. That agitation can be reduced by therapist behaviors including patience, a calm, purposeful approach, and a confident attitude. Explanation of the procedure to both parents and the child is essential and, in situations when NPPV is not required for life support, rewarding the child with scheduled breaks may markedly improve patient tolerance. If heavy sedation is required to control agitation or anxiety, NPPV outside of the intensive care unit is not practical.

Complications

Minor complications are commonly reported with NPPV and include local skin irritation, drying of the nasal and pharyngeal mucosa, nasal congestion, and eye irritation.[62] Skin irritation is the most common complaint and may be reduced by the use of special adhesives or by replacing the mask with nasal pillows. Mucosal drying can be reduced by adding a humidifier to the inspiratory circuit. Major complications of NPPV have not been reported frequently. Isolated case reports include pneumocephalus, bacterial meningitis, conjunctivi-

tis, massive epistaxis, and atrial arrhythmia as serious complications of nasal mask CPAP therapy.[10] Potential complications that have not been reported to date include pneumothorax and aspiration from gastric distention.

Compliance

Long-term compliance with NPPV in the domestic setting has not been systematically studied in pediatric-age patients. Compliance with nasal CPAP in adult patients with OSA is variable, ranging from 50-85%.[10] Adult patients who recognize that use of the device leads to symptomatic improvement are more likely to comply with nasal CPAP therapy. In a retrospective analysis of nasal CPAP therapy in children with OSA, compliance was described as inadequate in only 12/94, or 13%.[16] However, in another series of 20 pediatric-age patients, it was 65%.[63] Behavioral interventions focused on patient desensitization, parent education, and modeling are reported to improve compliance in pediatric patients treated with nasal CPAP.[64]

Treatment Criteria

Patient Selection

The decision to attempt NPPV in a child should be influenced by the available resources, diagnosis of the patient, and experience of the clinician. In the acute setting, NPPV may be helpful in children with acute hypoxemic respiratory failure as a means of avoiding intubation.[51,52] However, this approach has not been validated by controlled studies and has been used primarily in the intensive care unit. Application of NPPV in the pediatric general care areas and emergency room in children with acute respiratory dysfunction might be useful, but further studies are indicated. Clinicians who elect to use NPPV in children with acute respiratory distress should have a clear goal in mind, such as a reduction in inspiratory muscle effort or improvement in respiratory gas exchange, and document the outcome clearly in the medical record.

Children with chronic respiratory symptoms should be evaluated initially by a subspecialist experienced with pediatric respiratory disease to plan the appropriate diagnostic studies. We have found the sleep laboratory to be an ideal site to characterize the pattern of respiratory dysfunction and to study the effects of NPPV. Measurement of CO_2 elimination with a transcutaneous electrode or end-tidal monitor is essential to diagnose alveolar hypoventilation. In our hands, the transcutaneous method has been successful when the electrode is located on the anterior chest or abdominal wall and the measurement is correlated with a capillary or arterial blood gas sample.

Children with OSA accompanied by mild hypoxemia and normal CO_2 elimination can be treated with supplemental oxygen alone as a bridge to adenotonsillectomy. Nasal CPAP therapy should be considered in those children with more severe or prolonged hypoxemia, neurobehavioral abnormalities, sleep fragmentation, or known pulmonary vascular disease.[10] It can also be useful in children not cured by adenotonsillectomy or in those with complex anatomic anomalies that require staged surgical revision. NPPV may be useful in those patients in whom nasal CPAP therapy is not effective or is poorly tolerated.

Children with OSA associated with hypercarbia are a specific subset of patients who might benefit from NPPV. Whereas CPAP therapy can exacerbate central hypoventilation in such patients,[13,17] NPPV, in contrast, may increase tidal volume and improve respiratory gas exchange. However, the incidence of CPAP-induced hypoventilation is not well known; and NPPV is not a proven effective rescue therapy in children with nocturnal obstructive hypoventilation.

Children with chronic respiratory failure associated with neuromuscular disease or kyphoscoliosis are ideal candidates for NPPV in the domestic setting.[39] Children with neuromuscular disease may often have repeated episodes of partial or total airway occlusion during sleep which are manifest by polysomnography.[8] Treatment with negative pressure ventilatory-assist devices in children with neuromuscular weakness may actually potentiate obstructive apnea; thus, NPPV is likely to evolve as the preferred mode of therapy in this group of patients. Further experience is necessary to determine whether NPPV will defer tracheostomy in degenerative neuromuscular disease patients.

NPPV has been used in older children with central hypoventilation syndromes,[26,27] but its role as the primary mode of treatment in young patients is unconfirmed. In infants with idiopathic congenital hypoventilation, spontaneous restoration of brain stem responsiveness to CO_2 is unlikely. Thus, NPPV alone will probably not emerge as a long-term therapy for this condition.

Children with COAD, such as cystic fibrosis, may also benefit from nocturnal NPPV, especially in the advanced stages when there is respiratory muscle dysfunction and hypercarbia. However, controlled trials of NPPV in adults have not shown conclusive benefit. Children with severe COAD may require relatively high peak inspiratory pressures to overcome their ventilatory impedance; thus, devices with limited inspiratory pressure capability may not be as effective in this setting.[47]

Titration of Airway Pressures

Appropriate goals for the titration of airway pressures during NPPV include reduced inspiratory muscle effort, elimination of apnea and hypopnea, improved respiratory gas exchange, and improved sleep quality. The sleep laboratory is a site in which the physiologic response to NPPV can be critically examined. Two nights of study are typically required, the first night with unassisted ventilation to precisely categorize the pattern of respiratory dysfunction and the second night to apply NPPV and titrate the airway pressures. A one-

night study with a split protocol (baseline followed by NPPV) can be used to shorten the diagnostic evaluation, but this method has not been validated in children. This method is effective in titrating CPAP therapy in adults with OSA when the apnea/hypopnea index is high.[65]

Anecdotal experience suggests that relatively lower CPAP pressures may be effective in young children, but adolescents require levels of pressure similar to those used in adults.[10] In using flow-triggered devices to administer NPPV, the inspiratory pressure must exceed the positive end-expiratory pressure (PEEP) level by a sufficient magnitude to increase tidal volume, and PEEP should exceed 5 cm H_2O to avoid CO_2 rebreathing.[57] A wide range of inspiratory and expiratory pressure settings have been used in the pediatric application of NPPV with flow-triggered units.[21,22,45,52] We typically start pediatric-age patients on an expiratory pressure setting of 5-6 cm H_2O and inspiratory setting of 6-10 cm H_2O. The expiratory pressure can be adjusted upwards to improve oxygenation, and the inspiratory pressure can be increased to lower the P_{aCO_2} when necessary. In general, the difference between the inspiratory and expiratory pressure settings directly impacts the increase in tidal volume. In patients with chronic hypercarbia, it can be hours before the P_{aCO_2} falls in response to NPPV.

Patient Monitoring

I believe that children with chronic respiratory failure treated with NPPV should be seen every 2-4 months in a subspecialty clinic. Important variables that should be monitored include growth velocity and nutrition, muscle strength, swallowing function, daytime pulmonary function, and arterial blood gas values. The severity and expected progression of the underlying disease and the impact of growth velocity on mask size are all considerations in determining how often sleep studies should be repeated. A recent review of children with OSA suggested that mask CPAP pressures may need adjustment every 6-12 months.[16] Operations to restore upper airway patency are often followed by a variable period of tissue edema. Therefore, NPPV in these patients should be continued for at least 3-4 weeks following surgery before a repeat sleep study is repeated with the child off assisted ventilation.

In Summary

NPPV shows considerable promise as a safe and effective mode of therapy for children with respiratory dysfunction. NPPV has been reported in uncontrolled case series to be effective in pediatric patients with acute hypoxemic respiratory failure, nocturnal obstructive hypoventilation, neuromuscular weakness, and cystic fibrosis. However, specific clinical situations for children in which NPPV is proven to reduce morbidity, mortality, or cost compared to standard therapy are yet to be identified. To apply NPPV optimally in pediatric patients, the clinician should have a clear goal in mind, and document the child's response through analysis of the inspiratory muscle effort, respiratory rate, and respiratory gas exchange.

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Noninvasive Positive Pressure Ventilation: Predictors of Success and Failure for Adult Acute Care Applications

Dean Hess PhD RRT

Introduction
Controlled Studies
Intubation Rates
Length of Hospitalization & Cost
Survival
Uncontrolled Studies
Predictors of Success
Caregiver Issues
Ventilator & Patient Interface Issues
Patient Issues
In Conclusion

Introduction

Since 1990, there has been increasing interest in providing mechanical ventilation by noninvasive means to selected patients. This interest has been driven by the desire to avoid the complications of invasive ventilatory support, thus improving morbidity and mortality for patients in acute respiratory failure. The purpose of this paper is to review the reported success rates for noninvasive positive pressure ventilation (NPPV) for adult patients in acute respiratory failure and to review factors that have been shown to predict success or failure for this technique.

Controlled Studies

Seven controlled clinical trials of NPPV have been published since 1990.[1-7] Of these, 3 used historical controls[1-3] and 4 used prospective randomized controls,[4-7] with a total of 176 patients receiving NPPV and 179 receiving conventional therapy. Patients with chronic obstructive pulmonary disease (COPD) were studied predominantly, although 1 study specifically excluded patients with this diagnosis.[7] Pressure and volume modes of ventilation were used with critical care,[1,3,5] BiPAP,[2,6] and home care ventilators.[4] Some studies used nasal mask ventilation,[2,4,6] whereas others used full face masks.[1,3,5,7]

Intubation Rates

A primary outcome variable in controlled studies of NPPV has been the requirement for intubation, with a lower intubation rate in patients randomized to NPPV (Table 1). The overall rate of intubation in patients receiving conventional therapy was 54% (95% confidence interval of 47-61%) and only 23% (95% confidence interval of 17-29%) in patients receiving NPPV.

Length of Hospitalization & Cost

Some controlled studies have shown a reduced duration of hospitalization for patients receiving NPPV compared to those receiving conventional therapy (Fig. 1).[2,5] However, this was not a consistent finding.[4,6] Some studies have also reported a shorter intensive care unit stay for patients who received NPPV.[1,2]

Kramer et al[6] reported similar hospital charges for patients randomized to NPPV and conventional therapy. Criner et al[8]

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Table I. Summary of Controlled Studies of NPPV

Year	First Author	NPPV n	NPPV Intubated (%)	Control n	Control Intubated (%)	Mask	Ventilator	Pressure/Volume	Diagnosis
1990	Brochard[1]	13	8	13	85	Full	Critical care	Pressure	COPD
1993	Vitacca[3]	29	17	35	46	Full	Critical care	Pressure/volume	COPD
1993	Bott[4]	30	13	30	17	Nasal	Home care	Volume	COPD
1995	Brochard[5]	43	26	42	74	Full	Critical care	Pressure	COPD
1995	Kramer[6]	16	31	15	73	Nasal	BiPAP	Pressure	COPD, CHF, pneumonia, asthma, pulmonary embolism
1995	Wysocki[7]	21	62	20	70	Full	Critical care	Pressure	Pneumonia, cardiogenic pulmonary edema, laryngeal edema, chest wall disease
1996	Confalonieri[2]	24	8	24	38	Nasal	BiPAP	Pressure	COPD
	Total	176	23	179	54				

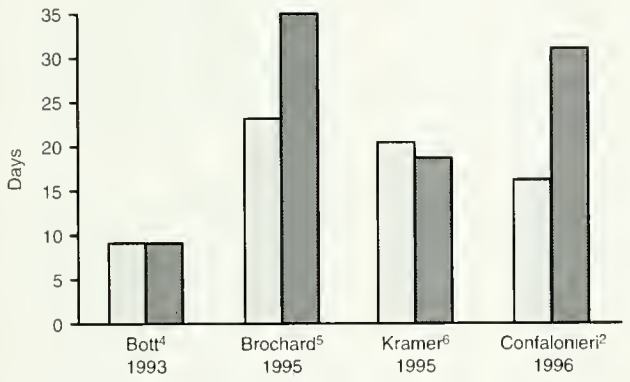

Fig. 1. Duration of hospital stay in days in 4 controlled studies of noninvasive positive pressure ventilation, NPPV (□) versus Control (■).

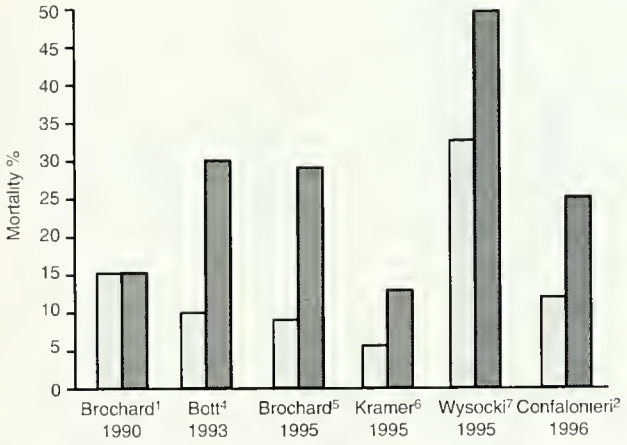

Fig. 2. In-hospital mortality (death rate) in 6 controlled studies of noninvasive positive pressure ventilation, NPPV (□) versus Control Group (■).

found that the present prospective reimbursement system does not adequately reflect the costs incurred using NPPV to treat patients with respiratory failure and substantial financial losses can occur when treating these patients. This may be related to the amount of time and effort required for successful application of NPPV. Nonetheless, NPPV may increase value because it improves quality of care for a cost similar to conventional therapy.

Survival

Controlled studies of NPPV have shown increased survival associated with this therapy (Fig. 2).[2,4-7] Moreover, Confalonieri et al[2] reported increased survival at 6 months (71% in patients who received NPPV and 54% in patients who received conventional therapy) and at 12 months (71% in patients who received NPPV and 50% in patients who received conventional therapy, Fig. 3).

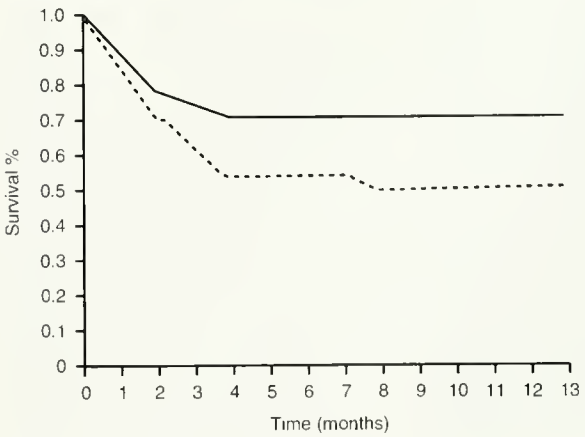

Fig. 3. Survival of patients receiving noninvasive positive pressure ventilation (solid line) and conventional therapy (broken line) in study reported by Confalonieri et al in 1996. (From Reference 2, with permission.)

Uncontrolled Studies

In addition to the controlled trials of NPPV, its use in about 700 acutely ill patients has been reported in uncontrolled trials (Table 2).[9-32] It is interesting to note that the overall success of NPPV in these uncontrolled studies is 75%—similar to that reported in the controlled clinical trials. The accumulated evidence in both controlled and uncontrolled studies strongly suggests that NPPV can avoid intubation in about 75% of patients.

In uncontrolled studies of NPPV, the predominant diagnosis has been COPD (Table 2). However, it should be noted that NPPV has been used successfully in patients with congestive heart failure (CHF), cardiogenic pulmonary edema, restrictive chest-wall disease, asthma, pneumonia, weaning from mechanical ventilation, and postoperative respiratory failure. Similar to the controlled studies, NPPV has been used successfully with both nasal and full face masks, and with volume and pressure ventilation. It has also been applied successfully with critical care ventilators, home care ventilators, BiPAP ventilators, and proportional assist ventilators.

The greatest number of patients treated with NPPV have been reported in a series of reports by Meduri et al.[9,21,30,31,33] This group uses a critical care ventilator with a full face mask

Table 2. Summary of Uncontrolled Trials of NPPV.

Year	First Author	Subjects	Success	Success Rate (%)	Mask	Ventilator	Pressure/ Volume	Diagnosis
1989	Meduri[9]	10	7	70	Full	Critical care	Pressure	COPD*, CHF, ARDS, cardiogenic pulmonary edema
1990	Carrey[10]	3	3	100	Nasal	Home care	Pressure	COPD, chest-wall disease
1990	Elliott[11]	6	5	83	Nasal	Home care	Volume	COPD, chest-wall disease, fibrothorax, cystic fibrosis
1991	Chevrolet[12]	6	3	50	Nasal	Home care	Volume	COPD, cystic fibrosis, restrictive lung disease
1991	Marino[13]	13	9	69	Nasal	Critical care	Volume	COPD
1991	Pennock[25]	29	22	76	Nasal	BiPAP	Pressure	Postoperative, ARDS, COPD, CHF
1991	Meduri[33]	18	13	72	Full	Critical care	Pressure	COPD, CHF, asthma, fibrothorax, pneumonia
1992	Folio[14]	25	24	96	Nasal	Critical care	Volume	COPD
1992	Benhamou[15]	30	18	60	Nasal	Critical care	Volume	COPD, CHF, asthma
1992	Udwadia[16]	22	18	82	Nasal	Home care or BiPAP	Pressure or volume	Variety of diagnoses; all patients weaning from mechanical ventilation
1993	Conway[17]	10	7	70	Nasal	Critical care	Volume	COPD
1993	Wysocki[18]	17	8	47	Full	Critical care	Pressure	COPD, postoperative, pulmonary fibrosis, cardiogenic pulmonary edema
1993	Fernandez[19]	14	11	79	Full	Critical care	Pressure	COPD
1993	Restrick[20]	14	13	93	Nasal	Critical care	Pressure or volume	Weaning from artificial airway of patients with COPD, postoperative, chest-wall disease, neuromuscular disease
1994	Meduri[21]	11	7	64	Full	Critical care	Pressure	Do-not-intubate with respiratory failure
1994	Confalonieri[22]	28	18	64	Nasal	BiPAP	Pressure	COPD
1994	Soo Hoo[23]	14	7	50	Nasal	Critical care	Volume	COPD
1994	Lapinsky[24]	2	2	100	Nasal	BiPAP	Pressure	Cardiogenic pulmonary edema
1994	Pennock[26]	110	88	80	Nasal	BiPAP	Pressure	Postoperative, COPD
1995	Chaing[27]	19	11	58	Nasal	BiPAP	Pressure	Patients with respiratory distress following extubation
1995	Ambrosino[28]	59	49	83	Full	Critical care	Pressure or volume	COPD
1996	Patrick[29]	11	8	73	Full/nasal	Proportional assist ventilation	Pressure	Pulmonary edema, sepsis, asthma, pneumonia
1996	Meduri[31]	158	112	71	Full	Critical care	Pressure	COPD, pulmonary edema, pneumonia, asthma, post-extubation
1996	Meduri[3]	17	16	94	Full	Critical care	Pressure	Status asthmaticus
1996	Pollack[32]	50	43	86	Nasal	BiPAP	Pressure	COPD, CHF, pneumonia, status asthmaticus
	Total	696	522	75				

*COPD = chronic obstructive pulmonary disease; CHF = congestive heart failure; ARDS = acute respiratory distress syndrome.

and has reported success (ie, improved gas exchange and avoidance of intubation) in patients with hypercapnic and hypoxemic respiratory failure with a variety of clinical diagnoses (Fig. 4). Although their work is uncontrolled, Meduri et al[31] have shown mortality rates in patients receiving NPPV that are less than predicted by APACHE II scores. They also report a low complication rate, the most common of which is facial skin necrosis.

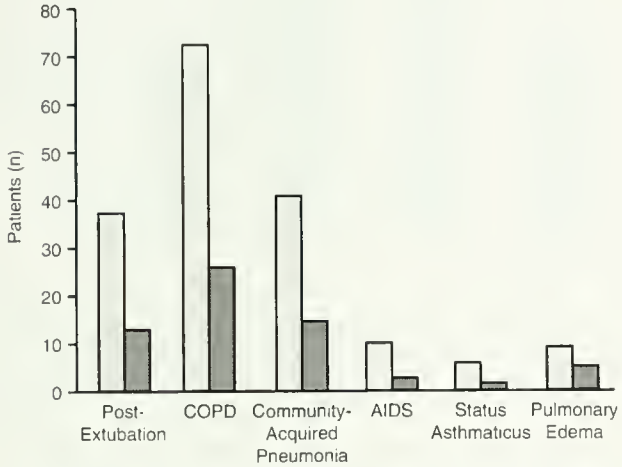

Fig. 4. Use of noninvasive positive pressure ventilation in patients with a variety of diagnoses, showing the total number of patients (□) and the number intubated (■) in each group. Graph is based on data from Reference 31.

Predictors of Success

Caregiver Issues

If NPPV is to be successful, those caring for the patient (physicians, nurses, respiratory therapists) must be committed to the approach. This is usually achieved by familiarizing these persons with the accumulated evidence suggesting that NPPV improves outcome in selected patients. Selection criteria and clinical application must be understood by those caring for these patients. Physicians must appreciate selection criteria; respiratory therapists must understand the issues related to ventilator management and selection of an appropriate interface; and nursing personnel must appreciate issues related to mask fit and skin care. Successful application of NPPV often begins with a clinical champion in the institution and may be facilitated by use of a dedicated respiratory therapist who conducts educational programs for clinical staff and supervises protocols for use of NPPV.[31]

Some clinicians are reluctant to initiate NPPV due to concerns related to time requirements and difficulties encountered when NPPV is initiated. Fitting the interface (mask), selection of appropriate ventilator settings, and patient coaching may be labor intensive for the first hours of NPPV. During the first 8 hours, Kramer et al[6] showed that the time requirement for respiratory therapists was greater for patients treated with NPPV than those intubated (Fig. 5). Therapists' time decreased significantly for the second 8 hours and was less for patients treated with NPPV than those who were intubated. It is interesting to note that Kramer et al[6] also found that nursing time was greater for the first 8 hours in those patients who were intubated and greater in the second 8 hours for patients who received NPPV. It has been my experience that the first hour of NPPV is labor intensive, but this time is well worth the benefit of avoiding intubation and a long course of invasive mechanical ventilation. I have also noted that the difficulties and time-intensity of NPPV decrease as the clinical team becomes more comfortable and familiar with this approach.

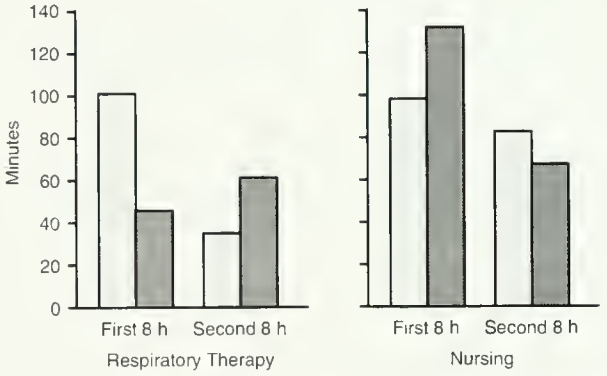

Fig. 5. Time requirements for respiratory therapy and nursing personnel to provide noninvasive positive pressure ventilation, NPPV (□) and Control (■). (From Reference 6, with permission)

Ventilator & Patient Interface Issues

A variety of ventilators and modes have been used successfully to apply NPPV (Tables 1 & 2). In patients with stable but chronic respiratory failure treated with nasal NPPV, Meecham Jones and Wedzicha[34] found no difference between two portable pressure support ventilators (BiPAP and Thomas NIPPY) and volume ventilators (BromptonPAC and Monnal-D). In patients with an acute exacerbation of COPD who were treated with nasal NPPV, Meecham Jones et al[35] reported no difference between pressure support ventilation (BiPAP) and volume ventilation (BromptonPAC). Elliott et al[36] compared nasal NPPV delivered by a volume ventilator or pressure support to 11 stable patients with chronic respiratory failure and found that both approaches substantially reduced inspiratory muscle work. It should be noted that these were short-term physiologic-response studies. To my knowledge, no published study has compared outcomes such as intubation rates and survival in patients randomized to different ventilators or modes for NPPV.

NPPV has been applied successfully using either nasal or full facial masks (Tables 1 & 2). To my knowledge, no published study has compared use of nasal and full face masks during NPPV for acute respiratory failure. The choice of interface, like the choice of ventilator and mode, is often based upon the bias and experience of the clinician. My personal preference is to use a full facial mask to initiate NPPV in patients with acute respiratory failure—when mouth leaks constitute a problem, then transition to a nasal mask after the initial acute phase. In practice, a variety of interfaces should be available, and the correct choice is often determined by trial and error.

Several studies evaluated the trigger and cycle characteristics of NPPV ventilators.[37-39] Although differences exist among ventilators, the clinical importance and impact on outcome are unknown. It is reasonable to use devices that trigger and cycle responsively to the patient's breathing pattern. It is also of benefit to use a device that compensates for leaks, which is a theoretical (but unstudied) benefit of the BiPAP and similar devices.

An issue that has generated considerable interest with the BiPAP device is the potential for CO_2 rebreathing. This is of particular concern for patients with acute hypercapnic respiratory failure. Ferguson and Gilmartin[40] reported significant rebreathing when BiPAP was used with its standard whisper swivel exhalation device, which affected the ability of the device to reduce P_{aCO_2}. Further, they found that CO_2 rebreathing could be effectively eliminated by use of a higher PEEP level ($\geq$ 8 cm H_2O) or a nonrebreathing exhalation valve. Lofaso et al[39] also found the degree of CO_2 rebreathing decreased when a higher PEEP level was applied.

Lofaso et al[41] compared pressure support through an artificial airway by BiPAP with a whisper swivel and with a nonrebreathing valve and by conventional critical care ventilator. Compared to the other methods, the BiPAP with whisper swivel resulted in similar arterial blood gas results but required a higher tidal volume, minute ventilation, and work of breathing. This was attributed to CO_2 rebreathing when the whisper swivel was used. The BiPAP with nonrebreathing valve prevented CO_2 rebreathing, but the additional expiratory resistance resulted in greater PEEP and more difficult triggering. In another study, Lofaso et al[39] found that larger esophageal pressure swings occurred when BiPAP with nonrebreathing valve was compared to a critical care ventilator, which they suggested was due to poor trigger sensitivity.

Whether rebreathing is important enough to affect outcome with BiPAP and similar devices that do not have separate inspiratory and expiratory lines is unknown. BiPAP has been used successfully to treat acute respiratory failure (Tables 1 & 2), including a prospective randomized trial.[6] It can be argued that the studies by Lofaso et al[39,41] are irrelevant relative to NPPV because they evaluated these devices in patients with artificial airways. Nonetheless, it seems prudent to use a ventilator and interface that minimize rebreathing during acute hypercapnic respiratory failure. Another issue related to rebreathing during NPPV is the volume of the interface (mask), which has not been clinically evaluated to my knowledge. In one study, an attempt was made to reduce the dead space by placing a foam insert into the mask.[5]

For acute care applications, it is also important to be able to precisely adjust the oxygen concentration that the patient receives (F_{IO_2}) and a modest level of oxygen supplementation may be needed. In my experience, this has been a limitation of the BiPAP and similar devices when used in the treatment of acute respiratory failure. With these devices, oxygen is administered by titrating it into the mask, resulting in an unknown and imprecise F_{IO_2}. The level of ventilator monitoring necessary during NPPV is controversial. Although the level of monitoring and the alarms available on critical care ventilators may be unnecessary, it seems prudent to at least monitor airway pressure and provide a disconnect alarm during NPPV.

An issue related to NPPV is the delivery of inhaled medications. If a critical care ventilator is used, aerosols can be delivered using the nebulizer control integral to the ventilator. Aerosols can also be delivered by nasal mask during BiPAP. Pollack et al[42] randomized patients with wheezing to aerosolized albuterol without or with BiPAP (inspiratory pressure of 10 cm H_2O and expiratory pressure of 5 cm H_2O) and found that the increase in peak expiratory flow was better when BiPAP was used—even with nasal inhalation of the drug. To my knowledge, use of MDI during NPPV has not been reported.

Patient Issues

Appropriate patient selection is an important predictor of success. Common selection criteria include acute respiratory distress (moderate to severe dyspnea, accessory muscle use, tachypnea) and hypercapnia (pH $\leq$ 7.35 and $P_{aCO_2} \geq$ 45 torr).[5-7,31] Some groups have also used NPPV to treat acute hypoxemic respiratory failure.[5,7,31] Commonly reported exclusion criteria include apnea or need for immediate intubation, hypotension (systolic blood pressure $\leq$ 90 mm Hg), uncontrolled dysrhythmias and/or evidence of myocardial ischemia, upper airway obstruction or facial trauma, inability to clear secretions, inability to cooperate, and facial deformity or other inability to fit the interface (mask).[5,6,31]

The strongest evidence of effectiveness of NPPV for acute respiratory failure comes from COPD patients with acute decompensation (Tables 1 & 2). Of 7 controlled trials of NPPV, 5 included only patients with COPD (Table 1).[1-5] Kramer et al[6] reported a more striking difference in intubation rates between NPPV and conventional therapy for patients with COPD (Fig. 6). Wysocki et al[7] excluded patients with COPD and found that the intubation rate was lower with NPPV than with conventional therapy only for patients who were hypercarbic (Fig. 6).[7] Although the strongest evi-

dence (ie, controlled clinical trials) suggests that NPPV is likely to be successful for patients with COPD and/or hypercapnic respiratory failure, it should be noted that NPPV has been used successfully in the treatment of hypoxemic respiratory failure.[31]

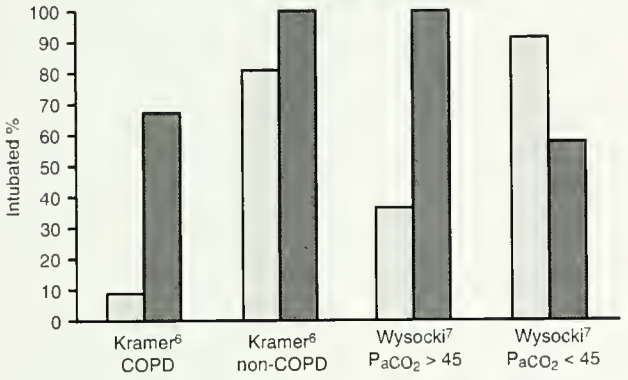

Fig. 6. Success of noninvasive positive pressure ventilation in patients with and without chronic obstructive pulmonary disease and with and without hypercarbia, NPPV (□) and Control (■).

The initial response to NPPV may predict success or failure. Brochard et al[5] found that most patients who failed NPPV were intubated within the first 12 hours of therapy. Soo Hoo et al[23] found that there was a more rapid decrease in P_{aCO_2} in patients where NPPV was successful, and Meduri et al[31] found that P_{aCO_2} increased in patients when NPPV failed and decreased in patients when NPPV was successful (Fig. 7). Meecham Jones et al[35] found that P_{aCO_2} tended to increase in patients treated with NPPV who had a baseline P_{aCO_2} > 65 torr, whereas P_{aCO_2} decreased when the baseline level was lower.

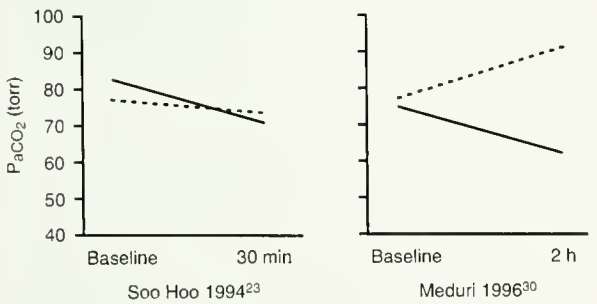

Fig. 7. Changes in P_{aCO_2} in patients who responded successfully (—) and those who did not respond (– –) to noninvasive positive pressure ventilation as reported in References 23 and 31. See text for details.

Two studies were designed specifically to identify determinants of success and failure of NPPV. Soo Hoo[23] used nasal NPPV delivered by a volume ventilator to 12 COPD patients in acute hypercapnic respiratory failure. Unsuccessful nasal NPPV was associated with greater severity of illness, greater mouth leak, and increased difficulty acclimating to NPPV (Table 3). The greater mouth leak was associated with patients who were edentulous, had excess secretions, and used pursed lips breathing. Ambrosino et al[28] used pressure or volume NPPV delivered through a nasal or full face mask to 47 patients with acute respiratory failure due to COPD. They found that 5 variables had a predictive value > 0.80 for distinguishing between success and failure of NPPV (Table 4). By logistic regression analysis, only baseline pH remained significant, with a sensitivity of 0.97 and specificity of 0.71. Success was greater for patients with a higher baseline pH, perhaps because low pH was a marker of more severe illness.

Table 3. Factors Predicting Success of Nasal NPPV in Patients with COPD (data from Reference 23).

Factor	Successful*	Not Successful	P Value
APACHE II Score	15 (4)	21 (4)	0.02
Exhaled Tidal Volume (mL)	757 (79)	514 (168)	0.002
Mouth Leak (mL)	100 (70)	314 (107)	0.002
Duration of NPPV (hr)	22.7 (15.6)	1.4 (1.6)	0.01

*Values are mean (SD).

Table 4. Predictability, Sensitivity, and Specificity of 5 Parameters of Success of NPPV in Patients with COPD (data from Reference 28).

Factor	Predictability	Sensitivity	Specificity
APACHE II Score	0.85	0.90	0.67
Neurologic Score	0.84	0.80	1.0
NPPV P_{aCO_2}	0.85	0.87	0.73
Baseline pH	0.08	0.87	0.54
NPPV pH	0.92	0.93	0.95

In Conclusion

NPPV is useful in decreasing the intubation rate in patients with acute respiratory failure. This is particularly the case for patients with COPD. The results of some studies also suggest a survival benefit for use of NPPV in patients with acute respiratory failure associated with COPD. More severely ill patients and those with excessive secretions, altered neurologic status, or hemodynamic compromise may be less likely to respond successfully to NPPV (ie, avoid intubation). The initial P_{aCO_2} change and mask tolerance may also be predictors of success. It is unknown whether technical issues such as type of ventilator, choice of pressure versus volume ventilation, and nasal versus full facial mask affect outcome for NPPV.

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Complications of Noninvasive Positive Pressure Ventilation

Nicholas S Hill MD

Introduction
Complications Related to the Interface
- **Nasal Masks**
- **Oronasal Masks**
- **Mouthpieces**

Complications Associated with Air Pressure & Flow
- **Nasal & Sinus Pain & Discomfort**
- **Gastric Insufflation**
- **Eye Irritation**
- **Pulmonary Barotrauma**

Threats to NPPV Continuation
- **Intolerance**
  - **Mask Intolerance**
  - **Patient-Ventilator Dyssynchrony**
- **Failure To Ventilate Adequately**
  - **Causes & Cures**
  - **Air Leaking**
  - **Rebreathing**

Major Complications
Avoidance of Complications
Summary & Conclusions

Introduction

The administration of positive pressure ventilation noninvasively (ie, via a mask or other interface, without the need for airway invasion) has been gaining popularity over the past decade for therapy of both acute and chronic forms of respiratory failure. Potential advantages of noninvasive positive pressure ventilation (NPPV) over invasive ventilation include avoidance of airway trauma, greater comfort, and preservation of airway defenses and speech and swallowing functions. Controlled studies in patients with acute respiratory failure due to chronic obstructive pulmonary disease (COPD) show that NPPV may be used to avoid intubation[1] and to lower complication and mortality rates.[2,3] For chronic respiratory failure, studies show long-term success rates comparable to those achieved with chronic invasive ventilation among patients with neuromuscular and restrictive chest-wall diseases.[4,5] These studies demonstrate that NPPV is generally safe and well tolerated, but some complications do occur. In this paper, I discuss complications and limitations occurring with the use of NPPV, beginning with those associated with the mask and positive pressure ventilation, those interfering with patient acceptance and adaptation, and those inherent to noninvasive techniques.

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Complications Related to the Interface

Interface-related problems are the most commonly encountered complications during NPPV. Different types of inter-

faces are used to administer NPPV, and the specific problems encountered depend on type.

Nasal Masks

The most widely used interface, particularly for chronic respiratory failure, is the standard nasal mask. Its popularity derives from its widespread commercial availability in numerous sizes and types and its high rate of patient acceptance for nocturnal ventilation. The standard nasal mask (Fig. 1) was initially developed for delivery of nasal continuous positive airway pressure (CPAP) to treat obstructive sleep apnea, but investigators soon learned that it also was an effective means of delivering positive pressure ventilation via the nose, mainly in patients with neuromuscular diseases and kyphoscoliosis.[6,7] The standard nasal mask consists of a triangular-shaped clear plastic cowl that fits over the nose and is connected to ventilator tubing. A soft rubber or silicone flange contacts the skin and creates an air seal. Alternative nasal masks include nasal 'pillows' or 'seals' that consist of soft rubber pledgets that insert directly into the nostrils (Fig. 2) or custom-fitted nasal masks made of prosthetic materials (Lifecare Inc, Westminster CO).

Fig. 1. Standard continuous positive pressure nasal mask (Respironics Inc, Murrysville PA) originally developed for sleep apnea patients but found to be effective for delivering positive pressure ventilation.

As shown in Table 1, the most common adverse side effect of all nasal mask types is discomfort at points of skin contact, related to the tension necessary to control air leaks. The pattern of discomfort varies with mask type, as might be surmised, with the standard nasal mask applying most pressure over the bridge of the nose and cheeks and nasal pillows applying most to the nares. To minimize this problem, proper fitting of the mask is essential, and the least strap tension that acceptably controls air leaks should be used. The smallest mask size that just encompasses the nose is usually best, and fitting is enhanced by using commercially available fitting

Fig. 2. Nasal 'pillows,' or 'seals,' with tubing and head and chin straps (Nellcor Puritan Bennett, Lenexa KS)—an alternative to the standard nasal mask.

gauges. (Respironics Inc, Murrysville PA). The most common error in administering nasal ventilation is to apply excess tension on the straps in an effort to minimize air leaking. Should this occur, the first step is to make certain that the mask is not too large. Next, the mask should be lifted entirely away from the face and repositioned to assure proper seating of the flaps. Forehead spacers should also be used and replaced at regular intervals to redistribute pressure away from the nasal bridge. Strap tension should be adjusted so that no fewer than two fingers can be accommodated under them. Alternatively, different strap systems such as skull caps or softer materials should be tried to enhance comfort. Masks with thin plastic flaps (Sullivan "bubble" mask, Resmed Inc, San Diego CA), or the addition of thin flaps over the standard mask (Comfort Flaps, Respironics Inc) may enhance sealing at lower strap tensions. Alternatively, nasal pillows (Nellcor Puritan Bennett Inc, Lenexa KS) or seals (Healthdyne Inc, Marietta GA) may be used to avoid pressure on the bridge of the nose and cheeks.

Pressure sores occur when excessive pressure is applied for too long, leading to ulceration of the nasal bridge in up to 10% of patients (Fig. 3).[4] Should ulceration occur, artificial skin (Duoderm, Bristol-Meyers-Squibb Inc, Princeton NJ) may be applied to the area to afford greater protection and efforts to minimize pressure redoubled. Once again, nasal pillows may be used to avoid contact with the bridge of the nose and cheeks, but patients may find these equally uncomfort-

Table 1 Adverse Effects of Interfaces and Possible Remedies

Interface	Adverse Effect	Remedy
Nasal and Oronasal Masks	Discomfort	Proper fit, adjust strap tension, change mask type
	Nasal bridge redness, pressure sores	Reduce strap tension, use forehead spacer, try nasal "pillows," use artificial skin
	Acneiform rash	Cortisone cream, alternative mask
Oronasal Masks	Impede speech and eating	Permit periodic removal if tolerated by the patient
	Claustrophobia	Choose clear masks with minimal bulk
	Aspiration	Exclude patients unable to protect airway; nasogastric tubes for patients with nausea and abdominal distention
Mouthpieces/Lip Seals	Interference with swallowing, salivary retention	Coaching, adaptation
	Pressure on lips, cheeks	Proper fit, strap adjustment
	Dental deformity	Orthodontic consultation
	Aerophagia	Simethicone, coaching
	Allergic reactions	Change prosthetic materials
	Nasal air leaking	Nose clips, pledgets
	Accidental disconnection	Appropriate alarms in ventilator-dependent patients

able because of pressure on the nares. In this situation, alternating between the 2 mask types may provide a solution. Acneiform rashes may occasionally occur at points of skin contact, particularly on the cheeks. These often respond to hydrocortisone cream or topical antibiotics. Some patients experience claustrophobic reactions with standard nasal masks that may be ameliorated with nasal pillows or newer masks that are more compact and use softer rubber for nasal sealing, such as the Monarch Minimask (Respironics Inc). However, this mask has not been tested with NPPV. With the wide variety of nasal masks commercially available, an acceptable mask assembly can usually be found, and custom fitting is rarely necessary.

Fig. 3. Nasal ulceration induced by excessive pressure from a nasal continuous positive airway pressure (CPAP) mask used to deliver noninvasive ventilation. The patient was elderly, had congestive heart failure, and used the mask continuously over a several day period. All factors may have contributed to ulceration.

Oronasal Masks

Oronasal masks cover both the nose and mouth (Fig. 4) and are preferred by some investigators for therapy of acute respiratory failure. Compared to nasal masks, oronasal masks may reduce air leaking through the mouth or under the mask. On the other hand, nasal masks permit speech and eating during use. Oronasal masks, like nasal masks, can cause discomfort at areas of skin contact and ulceration at the bridge of the nose. They may also cause more claustrophobic reactions, and air leaking at the point of contact with the lower jaw may be a persistent problem, particularly in edentulous patients. A risk associated with the use of oronasal masks is aspiration following vomiting because of vomitus retained in the mask. This concern has led to the recommendation that a nasogastric tube be used routinely with oronasal ventilation.[8] However, because the complication is unusual, nasogastric tubes are probably unnecessary unless patients have nausea and vomiting or abdominal pain with distention.

Mouthpieces

Lip seals, mouthpieces, and custom-fitted orthodontic devices have not been used as widely as nasal or oronasal masks, and fewer descriptions have been published. Nonetheless, successful application of NPPV via mouthpiece has been reported in a large number of patients with neuromuscular disease.[9] Common problems associated with lip-seal ventilation include discomfort caused by foreign material in the mouth and pressure from the lip seal, and difficulty swallowing, with retention of saliva. Pressure sores occur on the cheeks or gums when lip seals are strapped on too tightly. Air leakage around the lip seal or through the nose may impair efficacy, some-

Fig. 4. Oronasal mask (Spectrum, Respironics Inc) that is suitable for the delivery of noninvasive ventilation because it has a valve that prevents rebreathing and a rapid-release strap to be used in the event of ventilator failure. Note that it applies pressure to the bridge of the nose, can produce pressure sores, and depends on sealing over the mandible to prevent air leakage.

times necessitating insertion of nasal pledgets or the use of nose clips. In my experience, one patient developed severe hypoventilation when growth of a mustache and beard did not allow the lip seal to seal adequately. Many of these problems can be overcome with fitting adjustments and adaptation, but I have found that commercially available mouthpiece and lip-seal systems are less well tolerated by patients than are nasal masks. Nonetheless, some centers have reported excellent results with custom-made mouthpieces fitted by an oral prosthetist.[9] In addition to the listed adverse effects, these centers report occasional allergic reactions to the prosthetic materials, dental deformation, and aerophagia. They have reported 11 deaths associated with mouthpiece ventilation among 257 users with neuromuscular disease.[9] Some deaths occurred when the mouthpiece accidentally fell out in patients who were dependent on mechanical ventilation, so adequate monitoring and alarms for such patients are advisable.

Complications Associated with Air Pressure & Flow

Nasal & Sinus Pain & Discomfort

Air pressure in the nose and sinuses may cause pain, burning, coldness, or ear pain during the initiation of NPPV (Table 2). For this reason, I advise initiating NPPV with relatively low peak inspiratory pressures (8-12 cm H_2O). Pressures can then be gradually titrated upward as tolerated by the patient. Nasal congestion and dryness are also common complaints, sometimes occurring at different times in the same patient. Mouth drooling and dryness are also common, the latter usually associated with air leaking through the mouth. Nasal congestion usually responds to nasal steroids or antihistamine-decongestant combinations. Nasal congestion associated with upper respiratory infections probably interferes with the efficacy of NPPV, and topical vasoconstrictors may be useful temporarily during such periods. Nasal dryness, often associated with a sensation of cold or burning, may respond to use of topical saline or emollient sprays. Oral dryness may lessen in response to measures aimed at reducing mouth leaking, such as chin straps. However, if dryness fails to respond to these measures, humidifiers should be added to the breathing circuit. When pressure-limited ventilators are used, pass-over type humidifiers should also be used. In my experience, heat and moisture exchangers and bubble-through humidifiers increase ventilator circuit resistance, interfering with triggering and rendering ventilator pressure setting inaccurate. When dryness becomes severe, epistaxis sometimes occurs during nasal ventilation. This is treated with local measures and humidification. Petroleum jelly gently applied to the internal surface of the affected nares may prevent further episodes.

Table 2. Adverse Effects Associated with Air Pressure and Flow with Possible Remedies

Adverse Effect	Remedy
Noise	Obtain muffler, alternative ventilator
Nasal, sinus, or ear pain	Reduce pressure
Nasal dryness, coldness, burning, or epistaxis	Nasal saline or emollient, heated humidifier
Nasal congestion	Topical nasal steroids, anticholinergics, oral decongestant/antihistamines, topical decongestants (temporary)
Oral dryness	Chin straps, humidifier
Gastric insufflation	Reassurance, pressure reduction, simethicone
Eye irritation	Proper mask fit, alternative mask
Barotrauma, pneumothorax	Inflation pressure reduction, pleurodesis
Poor synchrony, autocycling	Consider ventilator with adjustable sensitivity and rise time

Gastric Insufflation

Gastric insufflation is reported in up to 50% of patients using NPPV,[10] but is rarely intolerable. This may be because the lower esophageal sphincter pressure is estimated to be 33 cm H_2O,[9] well above peak insufflation pressures commonly used for NPPV. Patients often note increased eructation or flatulence for a few hours in the morning after using NPPV at night, but the author has encountered only one patient who found

this symptom intolerable. This patient failed to improve after a gastric tube was placed, and eventually underwent tracheostomy (Fig. 5). Although her nocturnal symptoms of gastric hyperinflation improved after the switch to invasive PPV, her daytime symptoms persisted, suggesting that aerophagia unrelated to NPPV was responsible for some of her difficulty. Less symptomatic patients may respond to agents like simethicone or simply may tolerate the symptom without therapy.

Eye Irritation

Eye irritation is another adverse effect of air flow associated with the use of standard nasal or oronasal masks and has been reported in up to a third of patients.[10] It is caused by leakage of air under the mask on the sides of the nose lateral to the nasal bridge, where effective sealing is difficult. This is occasionally caused by excessive tightening of mask straps, and loosening the straps may control the leak. Soothing eye drops may bring some relief of irritation. Alternatives such as adding comfort flaps or trying a bubble mask or nasal pillows may correct the problem.

Pulmonary Barotrauma

Pulmonary barotrauma is a rare occurrence during NPPV, most likely because insufflation pressures are usually low (< 25 cm H_2O). I have encountered two patients, a sister and brother, who developed recurrent pneumothoraces while receiving NPPV, both after insufflation pressures had been increased (from 14 to 16 cm H_2O in one and 18 to 20 cm H_2O in the other). Both had apical blebs that likely precipitated the problem, but NPPV may have contributed. One patient required tube evacuation and sclerosis (Fig. 6), and the other required open pleurodesis.

Threats to NPPV Continuation

Intolerance—Causes & Cures

In both acute and chronic settings, a substantial minority of appropriately selected patients (perhaps 25-33%) has difficulty tolerating NPPV. Such intolerance threatens successful continuation of NPPV, and in both settings, mask intolerance is the most common reason. With patience and persistence, the experienced practitioner should be able to achieve success with many of these patients, but at the expense of additional time. Proper fit of the mask and optimization of the strap system should first be assured. Different mask sizes and types should be tried if the patient is unable to tolerate the initial choice. Some patients tolerate oronasal masks when nasal masks fail and vice versa. Attaching a bag that contains various mask types and sizes to ventilators used for NPPV assures

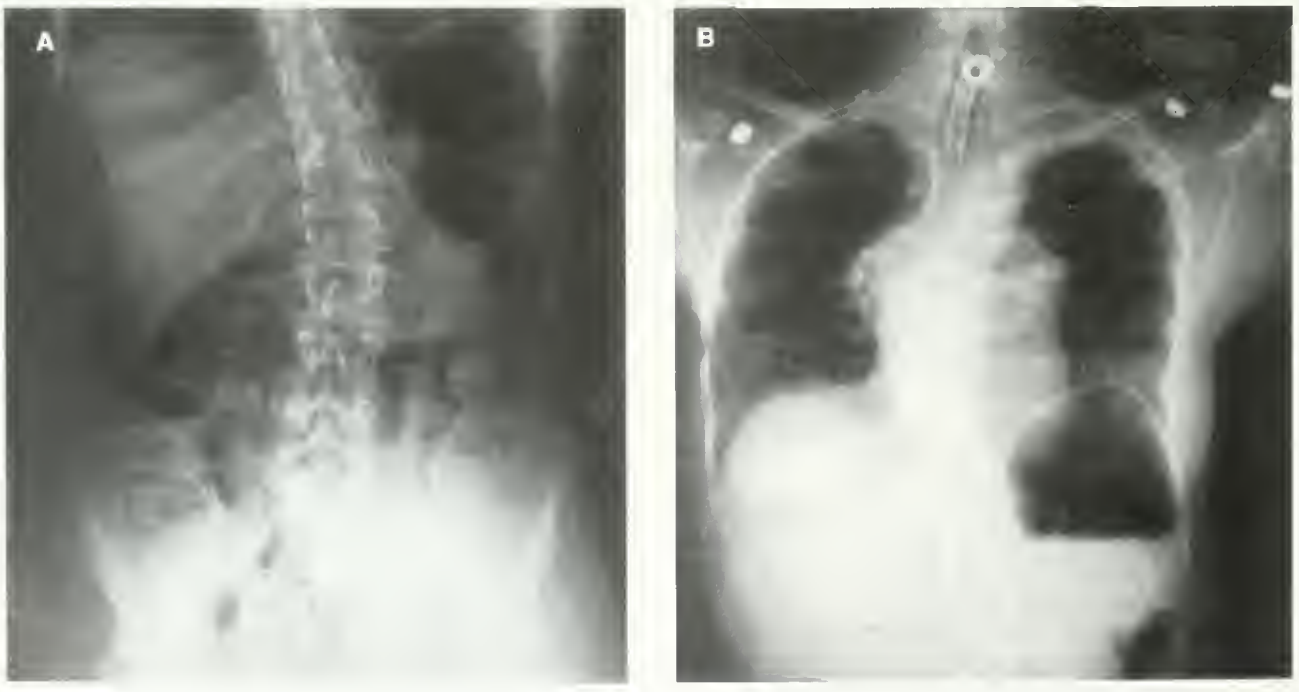

Fig. 5. A. Abdominal radiograph of 30-year-old woman using noninvasive positive pressure ventilation (NPPV) to treat respiratory failure caused by bilateral diaphragm paralysis associated with Charcot-Marie-Tooth disease. The large gas bubble visible in the stomach caused so much discomfort that a nasogastric tube was inserted in an attempt to alleviate it. B. Persistence of gastric insufflation despite replacement of NPPV by tracheostomy ventilation. Gastric insufflation was improved at night when she received ventilatory assistance but not during the day when she breathed spontaneously, demonstrating that part of her problem was caused by aerophagia and not by NPPV.

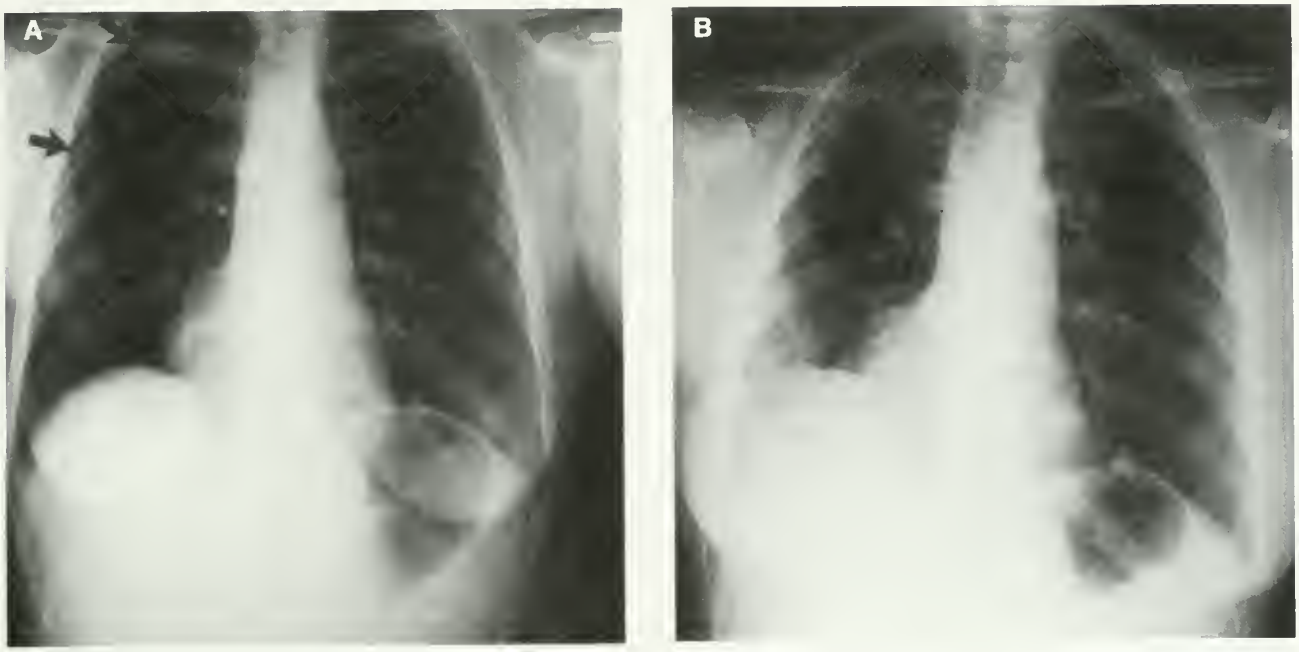

Fig. 6. A. Right pneumothorax (note pleural line indicated by arrows) in patient receiving noninvasive positive pressure ventilation, or NPPV, (BiPAP S/T, IPAP = 16 cm H_2O, EPAP = 4 cm H_2O, rate 16/min). The pneumothorax recurred after IPAP was lowered to 14 cm H_2O. B. Chest radiograph after chest-tube drainage and sclerosis of the right pleural space, which resulted in some worsening of chest-wall restriction and dyspnea.

ready availability. Other manipulations, such as adjusting body or head position may occasionally help.

Less often, failure to tolerate NPPV is related to difficulty with synchronization with the ventilator. Although volume- and pressure-limited ventilators appear to be similar in efficacy, some investigators have found that the pressure support mode is associated with fewer adverse side effects and is better tolerated.[11] Thus, switching to the pressure support mode may enhance synchronization and acceptance if the patient encounters difficulty on a volume-limited mode. Other ventilator adjustments, such as changes in pressure to optimize comfort, adding positive end-expiratory pressure (PEEP) in patients with presumed auto-PEEP, and silencing alarms in patients whose sleep is disturbed by them, are often useful in facilitating acceptance. With pressure-limited ventilation, attention must also be paid to adjustments that determine the termination of inspiratory support because low inspiratory-to-expiratory-time ratios or a too-sensitive expiratory trigger may shorten inspiratory times, leading to inadequate ventilatory assistance.[12]

In any case, the patient should be reassured and encouraged not to give up easily. Coaching the patient to adopt an appropriate breathing pattern and the suggestion "try to let the machine breathe for you" may be helpful. In the acute setting, judicious use of sedation may aid in acceptance. In the chronic setting, I discourage use of sedation and point out to patients that adapting to NPPV is not unlike learning to master a musical instrument. Frequent practice sessions are required, and months may pass before patients become expert at the technique. Despite all these efforts, however, some patients (perhaps 10-15%) remain unable to tolerate the sensation of a foreign object on the face or air flow in the nose or mouth (Table 3). In the acute setting, these patients may require intubation if respiratory failure persists. In the chronic setting, other forms of noninvasive ventilation, such as negative pressure or abdominal ventilation, may be successful if NPPV fails.[13]

Table 3. Approximate Frequency of Adverse Effects and Complications for Acute and Chronic Applications of NPPV* in Appropriately Selected Patients

Adverse Event or Complication	Frequency
Air leaking	100%
Nasal/oral dryness, congestion	25-70%
Mask discomfort	50%
Gastric distention	30-50%
Eye irritation	15-30%
Nasal redness/ulceration	10-20/5-10%
Aspiration	5%
Failure to ventilate	20%
Failure to tolerate	10%

*Ranges compiled from frequencies given in References 7-10, 23.

Failure To Ventilate Adequately

The inability to adequately assist ventilation causes failure of NPPV in 7 to 50% of patients (Table 3). In the acute

setting, this is most commonly related to failure to synchronize in patients who are agitated or unable to cooperate. Reassurance, coaching patients to let the ventilator breathe for them, and mild sedation may be useful in encouraging patients to permit the ventilator to assist in their work of breathing. Low initial inflation pressures or small tidal volumes that were selected to enhance patient comfort may also contribute to this problem. Gradual upward titration as tolerated by the patient may help in enhancing ventilatory assistance.

Inability to clear secretions and mucus plugging are other causes for failure to adequately ventilate. In patients with weakened expiratory muscles or severe restriction who have reduced peak cough flows, measures aimed at assisting coughing may help in secretion removal.[14] These include manually assisted coughing, during which a thrust to the midepigastrium using the palm of the assistant's hand is timed with coughing or use of mechanical devices like the In-Exsufflator (JH Emerson Co Inc, Cambridge MA). This device inflates the lungs with positive pressure (30-40 cm H_2O) via a face mask and then rapidly switches to a comparable negative pressure. However, when these fail or when swallowing is severely impaired, conversion to invasive ventilation is usually necessary. This potential complication underscores the importance of carefully screening candidates for NPPV for the ability to protect their airway.

In the chronic setting, failure to adequately ventilate may be caused by failure to successfully adapt, poor patient compliance, insufficient inflation pressures or delivered tidal volumes, excessive air leaking, or rebreathing. Some patients experience great difficulty adapting to NPPV and are able to use it for only an hour or two at bedtime. This is usually inadequate to effect sustained improvements in alveolar ventilation. In this situation, visits from a respiratory therapist can be helpful to evaluate mask fit and ventilator settings, and to make sure the patient is using the equipment correctly. The therapist tries alternative interfaces, reassures the patient that adaptation may be a lengthy process, and encourages the patient to gradually extend periods of nocturnal use. Some improvements in symptoms and gas exchange (as measured by blood gas values or daytime oximetry and end-tidal P_{aCO_2}) can be anticipated once the patient is using the device for at least 4-6 hours nightly. If no improvements are apparent, the patient should be encouraged to continue extending periods of use, and the ventilator timer should be checked to confirm reported hours of use. Inspiratory pressures or delivered tidal volumes should also be gradually increased as tolerated. If improvements remain inapparent (even after the patient is sleeping through the night using NPPV) and inspiratory pressures > 12 cm H_2O are being used, the patient should be monitored nocturnally using a multichannel recorder, seeking evidence of persisting hypoventilation, apneas, or excessive air leaking. Hypoventilation may respond to further increases in inflation pressure or duration of ventilation. Persisting obstructive apneas and hypopneas may be eliminated by adding PEEP to splint the upper airway open at the initiation of inspiration. Repeated nocturnal monitoring is indicated to ascertain whether the PEEP level is adequate.

Patient characteristics also influence the ability of NPPV to improve ventilation. Not surprisingly, those with severe restrictive thoracic or parenchymal lung disease are more difficult to ventilate successfully and may require higher inflation pressures than those with neuromuscular disease alone. Progression of the underlying process may also explain loss of effectiveness in patients previously stabilized with NPPV. Patients with slowly progressive neuromuscular diseases may experience gradual increases in daytime P_{aCO_2} as their respiratory muscles weaken, a process that can be slowed or prevented if upward adjustments are gradually made in inflation pressures and duration of ventilator use. Although many patients who initially fail to respond favorably to NPPV do respond to such measures, some do not. For these, alternative forms of noninvasive ventilation should be considered and may occasionally be successful. However, particularly in those with secretion retention due to weak cough or swallowing impairment, invasive ventilation will be necessary unless refused by the patient. In my experience, many patients with late-stage respiratory impairment agree to use NPPV but decline tracheostomy.

Air Leaking. Because there is no airtight conduit to the lower airways, NPPV is inherently leaky. Achieving a leak-free seal between mask and face is nearly impossible, but mask leaks can usually be reduced to acceptable levels. The greater challenge is to achieve adequate alveolar ventilation while relying on upper airway structures to permit air entry into the lungs. Awake, cooperative subjects can usually be coached to allow insufflated air to assist their breathing, but this is nearly impossible in agitated, uncooperative patients. During sleep, the success of NPPV depends on the continued patency of the upper airway. The question might be posed How do sleeping subjects permit insufflated air to enter their lungs? Mechanisms by which this is achieved are not fully understood, but recent studies offer some insight. Jouniaux et al[15,16] recently demonstrated that during both wakefulness and sleep, glottic aperture is an important determinant of air entry into the lungs. As compared to the awake state, this aperture narrowed slightly during Sleep Stages I and II and widened during deeper stages of sleep. In addition, increases in delivered tidal volume and reduced end-tidal P_{CO_2} correlated with narrowing of the aperture, reducing the proportion of air entering the lungs. Thus, glottic narrowing is one mechanism contributing to air leaking through the mouth. However, other mechanisms may be important, such as positioning of the soft palate and mandible.

Some leaking of air, either around the mask, through the mouth with nasal ventilation, or through the nose with mouth ventilation, is universal during NPPV. In a recent study, air leak through the mouth was noted during most of sleep in 7 patients with kyphoscoliosis receiving volume-limited nasal ventilation.[17] An association was detected between air leak

and sleep fragmentation, characterized by lightening of sleep stage and brief arousals. These arousals were most apt to occur during brief oxyhemoglobin desaturations associated with leaking, so hypoxemia was presumed to be the mechanism for the arousals. A more recent investigation on 6 patients (most with neuromuscular disease) who were using pressure-limited ventilation, also found leak during most sleep.[18] The prevalence of leaking was associated with sleep stage, occurring less often (62%) during Stage-1 sleep and most often (100%) during slow wave sleep (SWS, Stages 3 and 4). This latter study also found an association between air leaking and arousals, with arousals usually occurring at the end of periods of leaking and seeming to terminate them. However, oxyhemoglobin desaturations were not associated with the arousals, suggesting that they were caused by other mechanisms, such as noise, sensation of air flow, or perhaps increases in P_{aCO_2}. In fact, oxygen saturation was maintained above 90% throughout the night in all but one subject despite the air leaking, perhaps because the pressure-limited ventilator used (BiPAP S/T, Respironics Inc) can compensate for air leaks.

It is interesting to note that arousals were least apt to occur during SWS despite the prevalence of leaking, suggesting a diminished arousal threshold during this deeper stage of sleep. In addition, patients with frequent leak-associated arousals during Sleep Stages 1 and 2 rarely entered deeper stages of sleep, whereas those with infrequent arousals had substantially higher proportions of SWS and rapid eye movement, or REM, sleep. This suggests that having a high arousal threshold or the ability to habituate to arousals is conducive to sleep of better quality.

These studies demonstrate that although air leaking is highly prevalent during use of NPPV, it does not always impair efficacy. Ventilation and oxygenation may be adequately supported despite prolonged periods of leaking, depending on the ventilator used and adaptive mechanisms of the patient. Sleep fragmentation due to leak-associated arousals appears to be the major adverse consequence of leaking in most patients. However, when it is apparent that ventilatory assistance is being compromised by leaking, switching to a ventilator that has good leak-compensating capabilities (such as a portable pressure support ventilator) may help. In addition, adding chin straps may reduce leaking through the mouth during nasal ventilation. Alternatively, switching to an oronasal mask or mouthpiece may ameliorate the problem, although leaking can occur with any mask type. Based on the findings of Jouniaux et al,[16] increasing insufflation pressure or tidal volume to compensate for leaks may not always be the best strategy because this can lead to glottic narrowing and exacerbation of leak. Firm recommendations on the best way to deal with air leaking await more studies on compensatory upper airway mechanisms and the consequences of leak.

Rebreathing. Rebreathing may interfere with the effectiveness of ventilatory assistance when portable pressure support ('bi-level') ventilators are used. The phenomenon was first described during use of the BiPAP S/T (Respironics Inc), which uses a single ventilator tube for both inspiratory and expiratory flow.[19] The BiPAP and other bi-level ventilators use bias flow during exhalation to flush exhaled CO_2 out through fixed exhalation valves in tubing near the mask. Use of the BiPAP with the so-called whisper-swivel exhalation valve was shown to induce substantial rebreathing when expiratory pressures were low (< 4 cm H_2O). The rebreathing was enough to prevent CO_2 reduction in patients during a brief daytime trial. Subsequently, others[20] have demonstrated rebreathing with other bi-level ventilators, including the Companion 320 (Nellcor Puritan Bennett Inc, Lenexa KS) and Ventil+ (Sefam-Puritan Bennett, Nancy, France). The problem may be ameliorated by maintaining adequate bias flows with expiratory pressures > 4 cm H_2O or by using other exhalation valves, such as the Plateau or NRB (nonrebreathing) valves (Respironics Inc).

It is well to keep in mind, however, that currently available studies on rebreathing are based on laboratory investigations, and it is unclear how often rebreathing actually impairs the efficacy of bi-level ventilation in chronic at-home users. Our preliminary investigations show no improvement in nocturnal gas exchange among nasal BiPAP users when the Plateau valve is substituted for the whisper-swivel valve. This suggests that rebreathing is usually not an important problem during nocturnal use of BiPAP, perhaps because air leaking through the mouth is so prevalent that much of the exhaled CO_2 escapes orally. Rebreathing may be of more concern when NPPV is administered via the oronasal or oral routes when air leaking may be less, but this has not been evaluated.

Major Complications

It is fortunate that complications leading to clinically important medical morbidity are unusual with NPPV if the modality is reserved for appropriately selected patients. The most common significant complication among reported series on acute respiratory failure has been aspiration pneumonia, occurring in up to 5% of patients. This reflects the lack of airway protection afforded by the modality and the reliance on the patient's innate protective mechanisms. In my experience, this is an infrequent complication, seen most often in patients who are reluctant or decline to undergo endotracheal intubation and may have some impairment of airway protective mechanisms, but desire a trial with noninvasive ventilation nonetheless (Fig. 7).

Other major complications in the acute setting include mucus plugging, hypoxemia, and respiratory arrest. Mucus plugging can be minimized if patients are kept well hydrated and cough assistive techniques are used in patients with reduced peak expiratory flows.[14]

Hypoxemia during NPPV may occur as a consequence of mucus plugging, but adequate oxygenation is usually not di

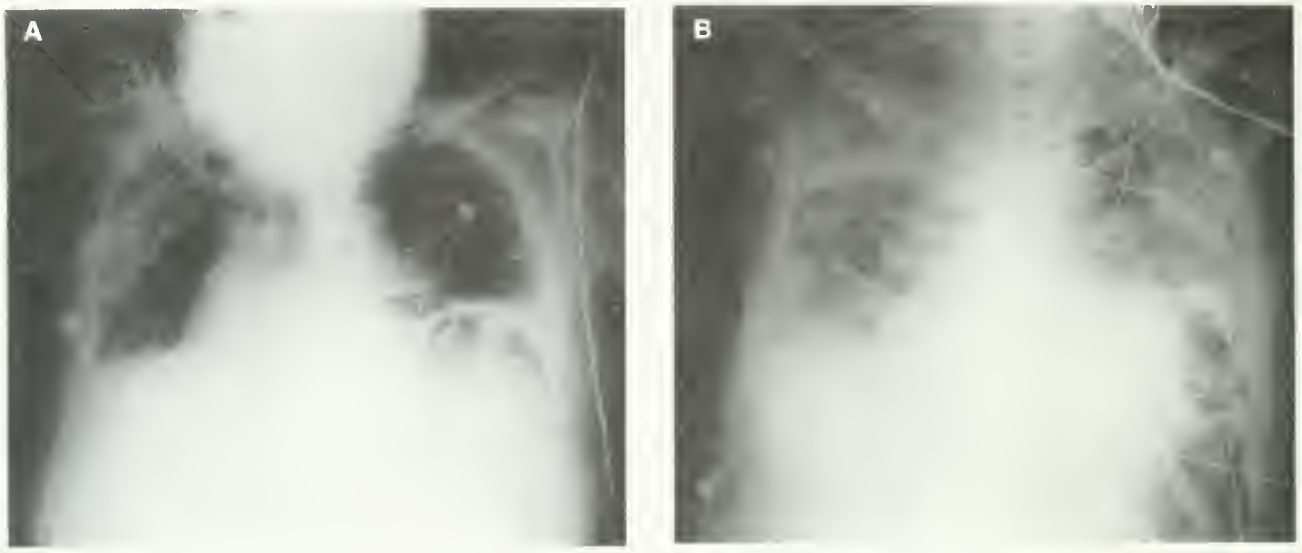

Fig. 7. A. Chest radiograph of a 77-year-old man with chronic respiratory failure caused by scoliosis and hemidiaphragmatic weakness resulting from surgical replacement of his left hemidiaphragm with a wire mesh 40 years earlier. He was admitted with worsening of his respiratory failure caused by an acute bronchitis and was stabilized with continuous noninvasive positive pressure ventilation (NPPV). B. The patient in 5A after an episode of aspiration that occurred during NPPV and resulted in development of acute respiratory distress syndrome. Despite intubation and ventilatory support, he died a day later.

ficult to achieve in patients with COPD exacerbations. With bi-level ventilators, oxygen tubing is connected directly to the mask or to a tap into the ventilator circuit, and flow is titrated upward until an adequate oxygen saturation has been achieved. Problems with oxygenation are more likely to occur if the patient fails to keep the mask on or if NPPV is administered to patients in hypoxemic respiratory failure (acute pneumonias or acute respiratory distress syndrome, or ARDS). Although success in some of these patients has been reported,[21] the safe and effective delivery of NPPV to such patients has not been established. Having a low threshold for conversion to invasive ventilation is prudent if these patients are proving difficult to manage noninvasively. It is obvious that immediate intubation is warranted in patients suffering a respiratory or cardiac arrest during NPPV use. This usually reflects a major cardiopulmonary crisis such as central airway obstruction, 'flash' pulmonary edema, or circulatory failure. The risk of these developments underlines the need to closely monitor acutely ill patients who are receiving NPPV until their condition has stabilized.

Hypotension is infrequent among appropriately selected patients receiving NPPV and is rarely attributable directly to ventilator use because of the relatively low pressures used. However, because even mild increases in intrathoracic pressure may decrease venous return and cause hypotension when intravascular fluid volume is low, the practitioner's first task is to make certain that fluid volume is adequate when hypotension occurs during NPPV use. If it occurs in a patient with a COPD exacerbation, one consideration is the possibility of the development of auto-PEEP. The patient should be coached to slow his breathing if he remains tachypneic. Shortening the rise time (in ventilators that have this capability) may allow more time for exhalation. If hypotension and evidence of organ hypoperfusion persist despite these measures, intravenous pressors can be initiated, but I favor prompt intubation and controlled breathing to minimize oxygen consumption by the breathing muscles.

CPAP has been shown to favorably affect hemodynamics in patients with cardiac failure,[22] but this depends on relative effects on preload and afterload. By increasing intrathoracic pressure in patients with high preload and afterload, CPAP can lower preload by decreasing venous return, and afterload by reducing the pressure difference between the thorax and peripheral vasculature. However, if preload is lowered excessively by increases in intrathoracic pressure, organ perfusion can be adversely affected. This could explain a recent observation on patients with acute pulmonary edema randomized to receive CPAP (10 cm H_2O) or BiPAP (15 cm H_2O inspiratory and 5 cm H_2O expiratory pressures). In this study,[23] patients on BiPAP had a more rapid improvement in ventilation and respiratory rate than patients on CPAP, but they also had a more abrupt decrease in blood pressure, associated with a higher rate of subendocardial myocardial infarctions. Although some of the BiPAP patients may have begun infarcting before admission, this finding underscores the need for caution in selecting initial pressures and close monitoring of hemodynamics when using NPPV in patients at risk for cardiac ischemia.

Avoidance of Complications

Although a knowledge of potential complications is essential in the successful management of patients on NPPV, the best course of management is to anticipate and avoid complications altogether, if possible. In this regard, a thorough familiarity with masks and strap systems is helpful. With nasal masks, one of the most common errors is to use a mask that is too large and then to tighten the straps excessively in an attempt to reduce air leakage into the eyes. Careful attention to optimizing mask fit and minimizing strap tension usually eliminates this problem. Also of critical importance is gaining experience in the implementation of NPPV and being able to share this experience with patients. Noninvasive ventilation affords patients a high degree of control over ventilatory assistance, but using it successfully requires learning. They must learn to relax their breathing muscles and position their upper airway structures to permit airflow into the lungs. This may be particularly difficult for patients in acute respiratory distress. Having an experienced practitioner available who can spend the time to optimize comfort and to coach them to relax and synchronize their breathing with the ventilator often makes the difference between success and failure.

Another important aspect of avoiding complications during use of NPPV is to exclude inappropriate patients. The likelihood of failure is so high in certain situations as to render a trial of NPPV worthless, and certain patients with respiratory failure could be harmed if invasive ventilation is inappropriately delayed. Patients with respiratory arrest or those who are agitated and uncooperative cannot be successfully ventilated noninvasively, so prompt intubation is warranted. Likewise, the inability to protect the airway presages certain failure. This determination requires judgment, however, and a trial of noninvasive ventilation may still be worthwhile in patients who have mild swallowing dysfunction. Patients with other unstable medical conditions, such as hypotensive shock, uncontrolled cardiac ischemia or arrhythmias, or active upper gastrointestinal bleeding, should also be promptly intubated to assure control of the airway and rest of the respiratory muscles. These exclusions eliminate the majority of patients in acute respiratory failure from consideration, but a recent study[24] found that 23% of patients entering an emergency department in acute respiratory failure still qualified for a trial of NPPV.[24] The exclusion criteria may be modified for do-not-intubate patients because there is little to lose by a trial. On the other hand, resources and time are wasted and hopes falsely raised if NPPV is used without some justification.

Summary & Conclusions

Noninvasive positive pressure ventilation is safe and has few major complications when used in appropriately selected patients. The most frequently encountered adverse effects are related to the mask and to air pressure and flow. These depend on the type of interface and ventilator used and include discomfort, pressure sores on the nasal bridge, dryness and congestion, and pain and burning in the nasal passages and sinuses. An important minority of patients fail to tolerate or ventilate effectively using noninvasive ventilation, but the number can be minimized by careful attention to mask fit and patient comfort and by giving patients adequate time to adapt. Technologic improvements in interfaces and ventilators are likely to further lower intolerance rates. Air leaking, mainly through the mouth, occurs commonly during use of nasal NPPV, may occasionally interfere with the ability to assist ventilation, and appears to impair sleep quality. Rebreathing associated with bi-level-type ventilator use may also interfere with ability to ventilate effectively but has not been studied sufficiently outside the laboratory setting to fully understand its clinical importance. Major complications of NPPV, including aspiration pneumonia, hypotension, barotrauma, and respiratory arrest, are unusual. Exclusion of inappropriate candidates and careful attention to patients during initiation help to minimize complications and assure the optimal use of NPPV.

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Study Design in the Evaluation of Noninvasive Positive Pressure Ventilation

Gordon D Rubenfeld MD MSc

Why Study?
Why Is NPPV Like Lung Volume Reduction Surgery?
The Research Question
- **Safety**
- **Clinical Utility**
- **Utilization**
- **Cost**

Study Limitations
- **Generalizability**
- **Bias**
- **Confounding**

Study Designs
- **Retrospective versus Prospective**
- **Nonexperimental Designs**
- **Experimental Designs**

In Conclusion

Why Study?

Although empiric research is one of the hallmarks of modern medicine, experts note that fewer than 20% of medical treatments have been validated by scientific studies demonstrating their efficacy.[1] It is possible that the proportion of respiratory care devices that have been shown to reduce morbidity or mortality is even less. Studies of noninvasive positive pressure ventilation (NPPV) provide information on its risks, benefits, and costs. Critical review of this body of evidence is essential for clinicians faced with the decision of using NPPV or selecting one particular device over another to provide NPPV. Government regulating agencies use these data to approve devices for public use. Insurers and other payers use study results to make decisions about reimbursement. Finally, expert panels draw on scientific studies to develop guidelines for the use of NPPV.

Investigators designing studies and critical readers of published studies are engaged in similar activities. Both must identify the research question, understand the strengths and limitations of various study designs, and appreciate the subtleties of bias, confounding, and statistical analysis. In this paper, I provide an introduction to these concepts based on clinical studies in patients, but many of the issues apply equally to animal and bench research.

Why Is NPPV Like Lung Volume Reduction Surgery?

NPPV and lung volume reduction surgery (LVRS), the surgical therapy that many believe offers patients with severe emphysema marked symptomatic improvement, may not seem like related treatments.[2] However, they share features that make

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them challenging study design problems. Neither investigators nor patients can be effectively blinded to either treatment. In both cases subjective end points, dyspnea and exercise tolerance for LVRS, and intubation for NPPV, make the lack of blinding more of a problem. The diseases under study, end-stage chronic obstructive pulmonary disease (COPD) in the case of LVRS and respiratory failure in the case of NPPV, involve heterogeneous populations with highly variable disease progression. Therefore, simple case series indicating successful treatment may indicate only that investigators have selected for inclusion in the series a subgroup with a good prognosis. Both treatments rely heavily on the experience and skill of providers. This means that the results of trials may not apply in settings in which the providers are less skilled than the investigators. In designing a study of LVRS or NPPV, it is important that the control arm receive a credible therapy. For LVRS, this may mean providing aggressive pulmonary rehabilitation to the control arm. In a study of NPPV, the control arm should receive optimal treatment for the underlying cause of respiratory failure and similar attention to other aspects of their medical care. Finally, LVRS and NPPV have advocates who may feel that currently available evidence makes a randomized trial unethical. All of these factors present serious but, once identified, surmountable obstacles to designing studies to evaluate NPPV.

The Research Question

The most important step in planning a study is developing a clear and specific research question. Research questions about NPPV address 4 general topics (Table 1).

Table 1. Research Questions To Evaluate Noninvasive Mechanical Ventilation (NPPV)

Aspect	Example
Safety	What are the complications of NPPV?
Clinical Utility	Does NPPV reduce the need for intubation? Does NPPV reduce mortality in acute respiratory failure?
Utilization	What percentage of hospitals offer NPPV as an option? Is the decision to use NPPV related to the percentage of managed care patients at the hospital or to the volume of patients in acute respiratory failure?
Costs	What are the costs of NPPV?

Safety

Safety studies describe the relative incidence and range of complications seen with NPPV. In addition, safety studies identify those patients who are at high risk of developing complications.

Clinical Utility

Clinical utility studies investigate the effect a treatment has on patient outcome in an attempt to justify the claim that the treatment is clinically useful. In framing the research question about clinical utility the investigator must choose an outcome to study (Fig. 1). Mortality is an unequivocal end point with indisputable clinical relevance. However, it is possible for treatments to be beneficial without reducing mortality. For example, treatments that improve quality of life, reduce discomfort, or decrease complications all are beneficial even if they do not reduce mortality. It is important that the outcome have clear relevance to clinicians or patients. Physiologic or biochemical end points may explain how a treatment works but do not demonstrate clinical utility. For example, a study that shows that NPPV reduces work of breathing but did not investigate its effects on mortality, length of stay, or patient comfort is inadequate to demonstrate clinical utility. Readers should critically evaluate studies that report only intermediate end points to decide whether they are clinically important and to judge the claims made by the investigator.

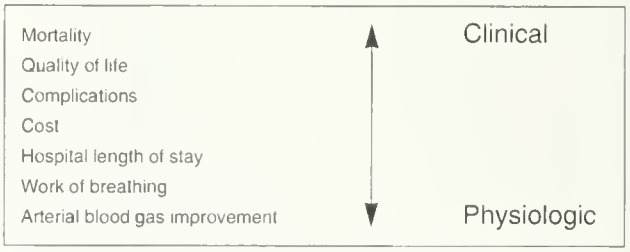

Fig. 1. The spectrum of clinical outcomes for use in clinical utility studies

In clinical utility studies that use intubation as an end point, NPPV is determined to be effective if it reduces the number of patients who require intubation. This end point has been accepted with little criticism in the literature. The presumption is that by avoiding intubation, patients are spared associated complications, such as nosocomial pneumonia and glottic injury. By avoiding complications associated with intubation and prolonged weaning from mechanical ventilation the overall duration and cost of hospitalization may be decreased. Finally, patients may find NPPV more comfortable than intubation. Critical readers should appreciate that a study that shows a reduction in intubation can only claim that NPPV reduces intubation. If the clinically important end points are pneumonia, cost, complications, or patient comfort, then these should be studied independently.

Utilization

Utilization studies investigate the factors that influence physicians' decisions to use diagnostic tests, treatments, and

admissions to the hospital.[3] Patient sociodemographics (age, gender, race, insurance), physician characteristics (location of practice, experience, training), and health care organization (open versus closed intensive care unit, managed care) may all play a role in clinical decision making. For example, a utilization study may study the relationship between managed care and use of NPPV hypothesizing that stimuli to cut costs may lead to the use of NPPV. There has been little or no utilization research on NPPV.

Cost

How much does NPPV cost? Costs are the total resources consumed in producing a good or service, expressed in currency. In calculating the costs of NPPV, it is important to evaluate the incremental costs of NPPV, which reflect the costs of NPPV compared to the alternative treatment. For example, if patients who receive usual care for COPD exacerbation are admitted to a standard hospital bed but NPPV patients require intensive care unit (ICU) monitoring, then the ICU costs must be added into the NPPV costs. Although cost is a useful concept, it may be difficult to actually measure costs. It is difficult to know what a day in the ICU actually costs; however, it is easy to find out what a given hospital charges payers for the day. Cost analyses frequently rely on what is charged or paid for a device or service as a proxy for cost, but those amounts can be unreliable because they vary from consumer to consumer. Hospital A may charge private insurers $1,500 for an ICU day but only charge a large managed care company $1,000. A cost analysis will yield different results depending on which of these charges is used. (The reader is referred to a recent paper[4] in the Journal for a more detailed discussion.)

Cost analyses also assume a perspective from which the cost model is calculated. Additional equipment and training costs incurred by providing NPPV are important in an analysis from the hospital's perspective, but not from the perspective of the insurance company that pays a fixed rate for each admission. Depending on whether the cost perspective is the patient's, the payer's, or society's, different cost figures can be obtained. There is no correct perspective, but the cost analysis should make the assumptions explicit in the report. Economic analysts perform sensitivity analysis to make their conclusions more robust in the presence of these uncertainties and assumptions. By recalculating the analysis and allowing key variables to assume different values within a range (for example, between $1,000 and $3,000 for a day in the ICU), the investigator can judge whether the cost model is sensitive to the assumptions. Sometimes the conclusions of the cost analysis are invariant across extreme variability in the assumptions. In such cases, readers can be confident in the model. Other studies will find that the analysis is sensitive to one variable, and attention can be directed toward obtaining more information about that specific variable. Given the number of assumptions that are made in a cost analysis and the lack of standardization in methodology, comparing figures from different studies can be problematic.[5] Efforts are underway to standardize the methods and terminology, which may help avoid these problems.[6,7]

Study Limitations

No study is perfect. The final product always represents trade-offs to accommodate fiscal constraints, patient availability, or specific research agendas. Whether one is reviewing a project proposal or reading the published results, attention should be directed to 4 aspects that may compromise a study's ability to answer the research question.

Generalizability

No matter how large the study, it can examine only a sample of patients who might receive NPPV in practice. If the study is generalizable, then its findings can reasonably be extended beyond this sample to other patients. How the subjects are selected, who provides the treatment, the setting in which the patients receive care, and how these details are reported in the publication all affect generalizability. Clinical utility studies use a special nomenclature for generalizability. Efficacy is the clinical utility of NPPV under ideal study conditions as performed by experienced personnel on a specific and usually narrowly defined patient population. Effectiveness is the clinical utility of NPPV as used in the community by a broad range of providers in a heterogeneous patient population. Studies that demonstrate efficacy may not be generalizable to conclusions about effectiveness.

Although it is important to recognize the limitations imposed by the choice of patient population and clinical setting, there is a role for studies with a narrow focus. NPPV may be effective only when used by experienced personnel in a specifically defined subset of patients. In addition, if NPPV is not safe or effective in select groups of patients, then it is not necessary or ethically justifiable to pursue questions further in larger more expensive studies.

Performing a study that generalizes to many different providers, ICUs, and diseases is a challenge that requires a large sample size from many centers including community hospitals. Because it is difficult to perform these studies, it is essential that less ambitious designs provide enough information for readers to judge whether the study applies to their own patients and capabilities. Variables that are important in this assessment include a detailed description of patient-selection criteria, the proportion of eligible patients who were actually enrolled and their diagnoses, a description of the ICU, and the training participants received prior to using NPPV.

Bias

Studies that lack generalizability may reach valid conclusions, but, unfortunately, these conclusions do not apply

outside the confines of the study. A biased study leads to false conclusions; therefore, the generalizability of a biased study is irrelevant. Bias is a systematic error that can be introduced at any phase of the study.[8] As stated earlier, potential biases enter into NPPV studies because the treatment cannot be blinded. Ascertainment of the outcome may be biased by knowledge of who received NPPV. For example, in a study that uses intubation as an end point, it is possible that the decision to intubate is biased by knowledge that the patient did or did not receive NPPV. In addition to bias involved in ascertaining the outcome, it is possible that patients receiving the study treatment also receive additional attention and therapy. This biases the study toward showing an effect from the treatment when this effect is actually due to other ancillary therapies.

To avoid bias investigators should structure the study so that decisions and observations are performed equally or at random. Blinding ensures that errors introduced are random and do not bias the study in a specific direction. A measurement, treatment, or patient selection performed by a blinded investigator cannot bias a study. If the treatment cannot be obscured, then other measures are necessary to minimize bias. Protocols that reduce the investigator's choices in any particular measurement or decision have 2 advantages. They minimize bias by ensuring that all patients are treated equally by protocol. Protocols also reduce variability, which improves the precision and statistical power of the study. Developing protocols and assessing compliance for complex clinical decisions like intubation can be difficult.

Confounding

Causality is an inference based in part on the observation of an association between 2 variables.[8,9] For example, to justify the claim that patients with acute respiratory failure treated with NPPV have lower rates of pneumonia than those treated with standard therapy, an investigator in a hypothetical study observes that the nosocomial pneumonia rate in NPPV patients is 50% less than in the control group. If a third variable actually accounts for the observed association, then the relationship between treatment and outcome is confounded. If, for example, patients who received NPPV were younger and had been in the hospital for a shorter period of time prior to their respiratory failure, then the lower pneumonia rates may be due to these variables. The relationship between NPPV and lower pneumonia rates is confounded by age and duration of hospitalization prior to respiratory failure.

There are 4 solutions to confounding: restriction, matching, adjustment, and randomization. Matching and restricting the patient population eliminate the problem by forcing the patients to be similar with regard to the confounder. Adjustment is a quantitative technique that mathematically controls for the confounding variable. A variety of methods including stratification and multivariate regression can be used to accomplish this. Regardless of the method, adjustment allows investigators to present an estimate of the association between two variables that removes the effect of the extraneous confounding variables. Randomization does not 'control' confounding as matching and adjustment do. Instead, randomization reduces confounding to a matter of chance which is reflected in the statistical p value. Imagine a randomized trial that showed that NPPV was associated with a 30% decrease in mortality ($p = 0.03$). The probability that this observed decrease in mortality or a larger one occurred because sicker people were, by chance alone, assigned to receive the device is, by definition, the p value, 0.03 (3%). Randomization does not eliminate confounding, but it quantifies the probability that it occurred. Randomization has the distinct advantage of relieving the investigator of the responsibility of identifying confounders because all variables, known and unknown, are randomly distributed between the groups.

Study Designs

No study design is perfect. Every completed research project reflects a series of compromises between feasibility, fiscal constraints, and scientific validity. In selecting a design from the many possible choices (Table 2), the investigator considers whether the limitations and costs outweigh the ability of the design to provide answers to the research question.

Table 2. Study Design Options

Nonexperiments
Case series
Cohort
Case-control
Experiments
Blinded randomized trial
Nonblinded randomized trial
Cross-over trial
Before-after trial
Cluster randomized trial

Retrospective versus Prospective

Although a retrospective study design is commonly considered a weakness and prospective design a strength, one design is not necessarily superior to the other. Rather than critique a study solely for being retrospective, readers should identify specific problems with generalizability, bias, or confounding. Retrospective and prospective refer to the time frame in which the study was performed. Retrospective designs rely on data already collected on patients or subjects to answer a new research question. Investigators using retrospective data must rely on the information, documentation, and patient identification performed by others. A common source of retrospective data in intensive care clinical research is the medical chart. Here the investigator is limited to the tests ordered

and information recorded by others for purely clinical purposes, which may introduce bias when the investigator uses the data later to answer a research question. Prospective studies collect data in real time for the specific purposes of the research question. These designs, which are more expensive and involved than retrospective studies, allow investigators to define and control every aspect of patient identification, data collection, and diagnostic test ordering.

Nonexperimental Designs

Study designs can be broken down into experiments, in which the investigator assigns patients to receive the treatment, and nonexperiments, in which the investigator has no control over who receives the intervention (Table 2). Nonexperimental designs include the case series, cohort, and case-control studies. The case series is simply a report on a collection of patients who received the treatment. Case series can address questions about safety and cost but are poorly suited to questions of clinical utility unless the outcome in a control group is uniform and known with certainty. In a case series, all patients would have received NPPV, and, therefore, explicit comparisons to standard care (clinical utility) are impossible. Several factors can strengthen case series. Detailed information about how the patients were selected, their diagnoses, and severity of illness helps readers judge whether the case series is generalizable. The patients should be either a consecutive or random sample of those who received NPPV. It is essential to provide some information, if only a count, about patients who were not included in the case series. Although these steps do not eliminate the possibility that the case series is biased by clinicians' selection of the patients for inclusion in the series, they provide readers with enough information to judge the extent such bias occurred.

A cohort is a group of patients who share some identifiable characteristic usually beginning with the word all. For example, all patients admitted to the ICU or all Medicare recipients who were hospitalized with a primary diagnosis of myocardial infarction between January 1, 1995 and December 31, 1996. The cohort is followed until a study end point, such as death or ICU discharge, occurs. Individuals within the cohort are assessed for the presence of an 'exposure.' In traditional epidemiology this exposure may be tobacco, an infectious source, or asbestos. In evaluating medical care, the exposure is to a treatment like NPPV. The association between this exposure and the outcome is expressed as a relative risk. The relative risk is the proportional increase in mortality or other study outcome in those with the exposure compared to the unexposed. The cohort study is an excellent design for answering safety, comparative performance, cost, and utilization questions. Cohort studies can be inefficient for studying rare events because they require the investigator to collect data on a large group of patients of whom only a few will eventually have an outcome of interest. One modification of the cohort study, the parallel cohort, takes a series of patients with the exposure and compares them to a group of patients selected because they did not receive the exposure. When the exposed and unexposed subjects come from separate time periods it is called a historically controlled study. In general, because parallel cohort studies rely on sampling separate populations (exposed and unexposed), they are subject to more complex sampling and selection biases than single cohort studies. A 1982 analysis of the record suggested that historically controlled studies are biased toward concluding that interventions are effective.[10]

Case-control studies are used less frequently in the evaluation of medical treatments.[11] Instead of identifying a cohort of patients, assessing them for their exposure status, and following them until outcomes occur, case control studies start at the outcome. To study the association of NPPV with mortality using a case-control study, an investigator might start with a case series of all patients admitted with respiratory failure who died and a control group of patients with the same diagnosis who survived. To study the factors that influence the decision to use NPPV, the investigator would begin with a case series of patients who received NPPV. After identifying the patients for the case series, control patients who do not have the outcome are identified. Case-control studies are efficient for studying rare outcomes because they do not rely on following a large group of patients until they develop the outcome. Like parallel cohort studies, case-control studies use 2 separate samples (cases with the outcome and controls that do not have it) and are, therefore, subject to subtle biases in their selection that single-sample cohort studies lack.

Experimental Designs

In an experiment, the investigator assigns, usually randomly, patients to receive monitoring or not. As noted earlier, the strength of random assignment is that it reduces confounding from known and unknown variables to chance. Blinding is added to randomization to minimize bias in the assessment of outcomes and in the provision of treatments other than the study intervention. In combination, the blinded randomized controlled trial (RCT) is the strongest available evidence for demonstrating a causal relation between a treatment and an outcome.

There are several limitations to the blinded RCT. Although randomization is ethically justified when there is equipoise (that is, equally strong pro and con opinions on a treatment's clinical utility in the medical community), it may still be difficult for individual clinicians and patients to subject decisions to a coin toss.[12] RCTs are expensive endeavors and may take several years to enroll patients and reach conclusions. Blinding, though an essential part of bias reduction in study design, is particularly problematic for studies of ventilator and other respiratory care treatments that may be difficult to blind. Except for community-based large, simple trials, most RCTs

are designed to answer efficacy questions and do not adequately address effectiveness.[13] Finally, because assignment is controlled by the investigator, utilization questions cannot be answered by RCTs.

Modifications to the blinded RCT attempt to circumvent some of the limitations introduced by blinding and random assignment.[14] When interventions cannot be blinded, other safeguards to prevent bias should be instituted. Clinical decisions can be guided by protocol and study end points can be assessed by an independent observer who is blinded to the subject's assignment. To alleviate the burdens of individual randomization, study designs can assign each individual to receive both the intervention and control (cross-over study) or assign every individual for a period of time to receive the intervention (before-after and cluster randomization). Cross-over studies have little relevance to the evaluation of NPPV and are best suited to the study of drugs with short half lives. The before-after study collects data on an ICU during a control period and then institutes an intervention applied to all patients for an intervention period. For example, a hospital collects data for 6 months on patients admitted with acute respiratory failure and then institutes an NPPV protocol for appropriate patients. The mortality and other outcome variables are compared for all patients with acute respiratory failure in both time periods. Cluster randomization is a multi-unit extension of this design that collects the same data for the control period and then randomly assigns some ICUs to apply the intervention and others to continue as controls. Although these designs may avoid the complexities incurred by randomizing individuals, they suffer from other limitations. Secular trends in mortality and treatments independent of the study intervention limit the utility of the before-after (within-group) comparison. The between-group comparison in cluster randomization (comparison between ICUs randomized to start the intervention and those who remain as controls) is limited by the effective sample size of the study. Because the unit of randomization is the ICU, the unit of analysis cannot be the individual subject. Therefore, the sample size is not simply the number of patients, and study power is often limited by the number of clusters that are randomized.[15]

To address the high cost and limited ability of RCTs to address effectiveness, investigators have turned to nonexperimental designs to evaluate clinical utility. This approach, called outcomes research, is receiving increasing attention. There is a great deal of appeal to using non-experimental designs to assess clinical utility. Outcomes research relies on the variability in everyday clinical practice, "experiments of nature", instead of random allocation. Large sample sizes can be accumulated by using computerized medical data sets. By including data on community practice, the effectiveness of treatments can be studied. Although experience with these techniques is growing, nonexperimental designs are subject to concerns about bias and uncontrolled confounding that experimental designs elegantly avoid. Perhaps the greatest of these is confounding by indication.[16] In the absence of assignment, patients who receive a medical treatment may be different in ways that are difficult to control. For example, in a nonexperimental "outcome" study of NPPV, patients who received NPPV are noted to have higher mortality than those who did not receive NPPV even after controlling for age, severity, and cause of respiratory failure. It is possible in this hypothetical study that some of the patients who were selected for NPPV refused intubation and other aggressive measures. Therefore, their deaths were due to an unaccounted-for variable—in this case, the refusal of other life-sustaining treatments. Variables like DNR (do not resuscitate) orders, failure of initial therapy, and physician uncertainty are not captured by standard severity of illness measures but may independently be associated with a poor outcome. Failure to control for confounding by indication can bias the study in either direction. Because of these limitations, it is unlikely that outcomes research will ever replace the blinded RCT as the primary study to document efficacy. However, as experience mounts, nonexperimental studies of clinical utility will complement and extend the findings from efficacy-oriented RCTs.

In Conclusion

Future studies of NPPV in acute respiratory failure should be directed toward answering 4 questions. Can NPPV reproducibly reduce mortality, complications, and costs compared to standard care or, alternatively, is avoiding intubation alone sufficient justification for using NPPV? Can NPPV be performed outside of an academic setting with acceptable results? What is the optimal device to deliver NPPV? Using a careful analysis that includes training time for staff and additional monitoring for patients who receive NPPV, what are the incremental costs (or savings) of NPPV compared to standard care? Answering these questions will clarify the risks, benefits, and costs of NPPV for clinicians and patients.

NPPV presents a number of challenges to investigators trying to answer these questions. Learning to design better studies and to critically interpret research rests on an understanding of the fundamentals of study design and statistical analysis. A strong evidence base for medical practice allows clinicians to better serve patients and more efficiently use resources. Noninvasive mechanical ventilation does not merit clinical use simply on the basis of making sense; its risks, benefits, and costs, like those of other medical interventions, need to be carefully and empirically demonstrated.

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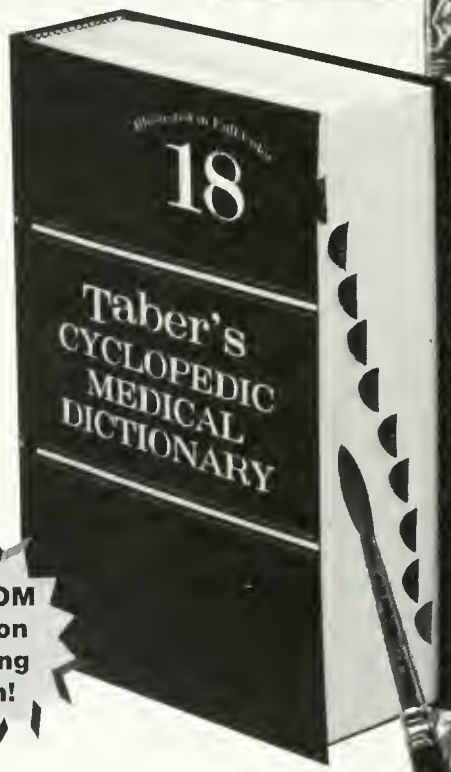

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An abstract may report **(1) an original study, (2) the evaluation of a method, device or protocol, or (3) a case or case series.** Topics may be aspects of adult acute care, continuing care/rehabilitation, perinatology/pediatrics, cardiopulmonary technology, or health care delivery. The abstract may have been presented previously at a local or regional—but not national—meeting and should not have been published previously in a national journal. The abstract is the only evidence by which the reviewers can decide whether the author should be invited to present a poster at the OPEN FORUM. Therefore, *the abstract must provide all important data, findings, and conclusions.* Give specific information. Do not write such general statements as "Results will be presented" or "Significance will be discussed."

Essential Content Elements

Original study. Abstract *must* include (1) Background: statement of research problem, question, or hypothesis; (2) Method: description of research design and conduct in sufficient detail to permit judgment of validity; (3) Results: statement of research findings with quantitative data and statistical analysis; (4) Conclusions: interpretation of the meaning of the results.

Method, device, or protocol evaluation. Abstract *must* include (1) Background: identification of the method, device, or protocol and its intended function; (2) Method: description of the evaluation in sufficient detail to permit judgment of its objectivity and validity; (3) Results: findings of the evaluation; (4) Experience: summary of the author's practical experience or a lack of experience; (5) Conclusions: interpretation of the evaluation and experience. Cost comparisons should be included where possible and appropriate.

Case report. Abstract *must* report a case that is uncommon or of exceptional educational value and must include (1) Introduction: Relevant basic information important to understanding the case. (2) Case Summary: Patient data and response, details of interventions. (3) Discussion: Content should reflect results of literature review. The author(s) should have been actively involved in the case and a case-managing physician must be a co-author or must approve the report.

Abstract Format and Typing Instructions

Accepted abstracts will be photographed and reduced by 40%; therefore, the size of the original text should be *at least* 10 points. A font like Helvetica or Geneva makes the clearest reproduction. The first line of the abstract should be the title in all capital letters. Title should explain content. Follow title with names of all authors (including credentials), institution(s), and location; underline presenter's name. Type or electronically print the abstract *single spaced in a single paragraph in the space provided on the abstract blank.* Insert only one letter space between sentences. Text submission on diskette is encouraged but must be accompanied by a hard copy. Identifiers will be masked (blinded) for review. Data may be submitted in table form, *and simple figures may be included provided they fit within the space allotted.* No figures, illustrations, or tables are to be attached to the abstract form. Provide all author information requested. A clear photocopy of the abstract form may be used. Standard abbreviations may be employed without explanation; new or infrequently used abbreviations should be spelled out on first use. Any recurring phrase or expression may be abbreviated, if it is first explained. Check the abstract for (1) errors in spelling, grammar, facts, and figures; (2) clarity of language; and (3) conformance to these specifications. An abstract not prepared as requested may not be reviewed. Questions about abstract preparation may be telephoned to the editorial staff of RESPIRATORY CARE at (972) 406-4667.

Deadline Allowing Revision

Authors may choose to submit abstracts early. Abstracts postmarked by March 17, 1997 will be reviewed and the authors notified *by letter only* to be mailed by April 25, 1997. Rejected abstracts will be accompanied by a written critique that should, in many cases, enable authors to revise their abstracts and resubmit them by the final deadline (May 27, 1997).

Final Deadline

The mandatory Final Deadline is May 27, 1997 (postmark). Authors will be notified of acceptance or rejection *by letter only*. These letters will be mailed by August 15, 1997.

Mailing Instructions

Mail (Do not fax!) 2 clear copies of the completed abstract form, diskette (if possible), and a stamped, self-addressed postcard (for notice of receipt) to:

RESPIRATORY CARE OPEN FORUM
11030 Ables Lane
Dallas TX 75229-4593

1997 Respiratory Care Open Forum
Abstract Form

18.8 cm or 7.4"

13.9 cm or 5.5"

1. Title must be in all upper case (capital) letters, authors' full names and text in upper and lower case.
2. Follow title with all authors' names including credentials (underline presenter's name), institution, and location.
3. Do not justify (ie, leave a 'ragged' right margin).
4. **Do not use type size less than 10 points.**
5. All text, tables, and figures must fit into the rectangle shown.
6. Submit 2 clean copies. This form may be photocopied if multiple abstracts are to be submitted.

Mail original & 1 photocopy (along with postage-paid postcard) to

Respiratory Care Open Forum
11030 Ables Lane
Dallas TX 75229-4593

Early deadline is March 17, 1997 (postmark)

Final deadline is May 27, 1997 (postmark)

Presenter

Name & Credentials

Mailing Address

Voice Phone & Fax

Corresponding Author if Different from Presenter

Name & Credentials

Mailing Address

Voice Phone & Fax

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For VOLUNTARY reporting by health professionals of adverse events and product problems

Page ____ of ____

Form Approved OMB No 0910-0291 Expires 4/30/96
See OMB statement on reverse

FDA Use Only (Resp Care)

Triage unit sequence #

A. Patient information

1. Patient identifier
In confidence

2. Age at time of event:
or
Date of birth:

3 Sex
☐ female
☐ male

4 Weight
____ lbs
or
____ kgs

B. Adverse event or product problem

1 ☐ Adverse event and/or ☐ Product problem (e g , defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
☐ death ____ (mo/day/yr)
☐ life-threatening
☐ hospitalization – initial or prolonged
☐ disability
☐ congenital anomaly
☐ required intervention to prevent permanent impairment/damage
☐ other: ____

3. Date of event (mo/day/yr)

4 Date of this report (mo/day/yr)

5 Describe event or problem

6. Relevant tests/laboratory data, including dates

7 Other relevant history, including preexisting medical conditions (e.g , allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

C. Suspect medication(s)

1 Name (give labeled strength & mfr/labeler, if known)
#1
#2

2 Dose, frequency & route used
#1
#2

3 Therapy dates (if unknown, give duration) (from/to or best estimate)
#1
#2

4 Diagnosis for use (indication)
#1
#2

5 Event abated after use stopped or dose reduced
#1 ☐ yes ☐ no ☐ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

6 Lot # (if known)
#1
#2

7. Exp. date (if known)
#1
#2

8 Event reappeared after reintroduction
#1 ☐ yes ☐ no ☐ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

9 NDC # (for product problems only)
– –

10 Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1 Brand name

2 Type of device

3 Manufacturer name & address

4 Operator of device
☐ health professional
☐ lay user/patient
☐ other: ____

5. Expiration date (mo/day/yr)

6.
model # ____
catalog # ____
serial # ____
lot # ____
other # ____

7. If implanted, give date (mo/day/yr)

8 If explanted, give date (mo/day/yr)

9 Device available for evaluation? (Do not send to FDA)
☐ yes ☐ no ☐ returned to manufacturer on ____ (mo/day/yr)

10 Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. Name & address

phone #

2 Health professional?
☐ yes ☐ no

3 Occupation

4 Also reported to
☐ [illegible]er
☐ [illegible]ility
☐ [illegible]ibutor

5 If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☐

FDA

Mail to: MEDWATCH
5600 Fishers Lane
Rockville, MD 20852-9787

or FAX to:
1-800-FDA-0178

FDA Form 3500 1/96)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

ADVICE ABOUT VOLUNTARY REPORTING

Report experiences with:

- medications (drugs or biologics)
- medical devices (including in-vitro diagnostics)
- special nutritional products (dietary supplements, medical foods, infant formulas)
- other products regulated by FDA

Report SERIOUS adverse events. An event is serious when the patient outcome is:

- death
- life-threatening (real risk of dying)
- hospitalization (initial or prolonged)
- disability (significant, persistent or permanent)
- congenital anomaly
- required intervention to prevent permanent impairment or damage

Report even if:

- you're not certain the product caused the event
- you don't have all the details

Report product problems – quality, performance or safety concerns such as:

- suspected contamination
- questionable stability
- defective components
- poor packaging or labeling
- therapeutic failures

How to report:

- just fill in the sections that apply to your report
- use section C for all products except medical devices
- attach additional blank pages if needed
- use a separate form for each patient
- report either to FDA or the manufacturer (or both)

Important numbers:

- 1-800-FDA-0178 to FAX report
- 1-800-FDA-7737 to report by modem
- 1-800-FDA-1088 to report by phone or for more information
- 1-800-822-7967 for a VAERS form for vaccines

If your report involves a serious adverse event with a device and it occurred in a facility outside a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

Confidentiality: The patient's identity is held in strict confidence by FDA and protected to the fullest extent of the law. The reporter's identity, including the identity of a self-reporter, may be shared with the manufacturer unless requested otherwise. However, FDA will not disclose the reporter's identity in response to a request from the public, pursuant to the Freedom of Information Act.

The public reporting burden for this collection of information has been estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to

DHHS Reports Clearance Office
Paperwork Reduction Project (0910-0291)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please do NOT return this form to either of these addresses.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • Food and Drug Administration

FDA Form 3500-back

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Department of Health and Human Services
Public Health Service
Food and Drug Administration
Rockville, MD 20857

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MEDWATCH
The FDA Medical Products Reporting Program
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20852-9787

Not-for-profit organizations are offered a free advertisement of up to eight lines to appear, on a space-available basis, in Calendar of Events in RESPIRATORY CARE. Ads for other meetings are priced at $5.50 per line and require an insertion order. Deadline is the 20th of the month two months preceding the month in which you wish the ad to run. Submit copy and insertion orders to Calendar of Events, RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229-4593.

Calendar of Events

AARC & AFFILIATES

April 15–16—Pennsylvania Society
32nd Annual Southeast District Seminar, "Happy 50th Respiratory Care," at the Airport Ramada, Essington, Pennsylvania.
Contact: Angie Herstine at (609) 784-0340 or Ann Cusano at (215) 646-7300 ext. 428.

April 16–18—Alabama Society
1997 Annual Respiratory Care Conference, "Educational Kaleidoscope," at the Radisson Hotel, Birmingham, Alabama.
Contact: (334) 705-3790 or (334) 434-3405, or e-mail toptholt@jaguar1.usouthal.edu

May 4–6—Washington Society
24th Annual Pacific Northwest Regional Respiratory Care Conference, at Cavanaugh's Inn and Convention Center, Yakima, Washington.
Contact: Richard Lawrson, 4448 200 78th Ave NE, Redmond WA 98053, (206) 880-4585.

May 20–21—Connecticut Society
Super Symposium, "Respiratory Care: The Magic Is in Your Hands," at the Four Points Sheraton, Waterbury, Connecticut.
Contact: Nancy Apruzzese, Director, Respiratory Care Services, at (860) 224-5264.

June 11–13—Texas Society
Annual convention, "The Star of Texas," at the Marriott Riverwalk Hotel, San Antonio, Texas.
CRCE: Credit has been requested.
Contact: TSRC at (972) 680-2454.

OTHER MEETINGS

April 12—University of Michigan Medical School
Conference, "Advances in COPD" at the Laurel Manor Conference Center, Livonia, Michigan.
3.5 credit hours in Category 1 of the Physician's Recognition Award of the American Medical Association; credit requested from the American Osteopathic Association.
Contact: Registrar, Towsley Center for Continuing Medical Education, Department of Postgraduate Medicine and Health Professions Education, University of Michigan Medical School, PO Box 1157, Ann Arbor MI 48106-1157.

May 8–9—Methodist Hospital/Clarion Health Partners Inc
International Conference on Multiskilling, at the Radisson Hotel City Centre, Indianapolis, Indiana.
Registration: $345 by April 1, or $395 after.
Contact: Lana Phillips at (317) 929-8925.

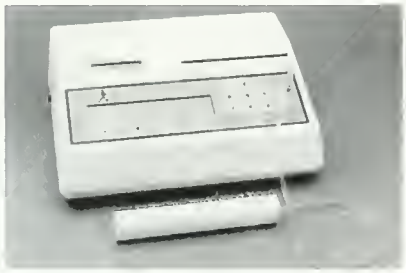
May 15–17—Miami Children's Hospital
Southeastern ECMO Conference, "Advances in Extraordinary Life Support," at Sheraton Yankee Trader Beach Resort, Ft Lauderdale Beach, Florida.
Contact: Karl Hultquist, Miami Children's Hospital, (305) 669-6423.

May 16–21—American Lung Association/ American Thoracic Society (ALA/ATS)
Annual International Conference in San Francisco, California.
Contact: 1997 International Conference, ALA/ATS, 1740 Broadway, New York NY 10019-4374, (212) 315-8808.

New Products & Services

News releases about new products and services will be considered for publication in this section. There is no charge for these listings. Send descriptive release and glossy black and white photographs to RESPIRATORY CARE Journal, New Products and Services Dept, 11030 Ables Lane, Dallas TX 75229-4593.

REUSABLE NEBULIZER. The PermaNeb, Model 700 pneumatic jet nebulizer, used with Pulmo-Aide® and Pulmo-Mate™ compressors, is issued by DeVilbiss Health Care Inc. According to the manufacturer, the PermaNeb cuts treatment time in half, delivers clinically effective particle size, and uses a novel mouthpiece and check-valve system. The system was designed for pediatric patients and features spill-proof operation for patients in either an upright or reclining position and is configured for standard 22-mm fittings for standard face masks or T-connector style mouthpieces. In addition, PermaNeb is reusable and top-shelf dishwasher safe. For clinic use, the system can be sterilized by autoclave. Circle Reader Service Number 160, for details from DeVilbiss.



SPIROMETER. A 2-in-1 spirometer is available through Vacumetrics Inc. The ATS-legal ChestTest spirometer works as a stand-alone spirometer capable of storing information for up to 50 patients, interfacing with personal computers that use Windows® software, and printing patient reports. The company also claims that the unit requires no cleaning, sterilization, or filter due to the unit's precalibrated, disposable flow transducers. The unit can also be used in pulmonary function tests. For this function, the ChestTest uses the precalibrated flow transducer and provides step-by-step instructions for all users. To learn more about the 2-in-1 spirometer, circle Reader Service Number 161.

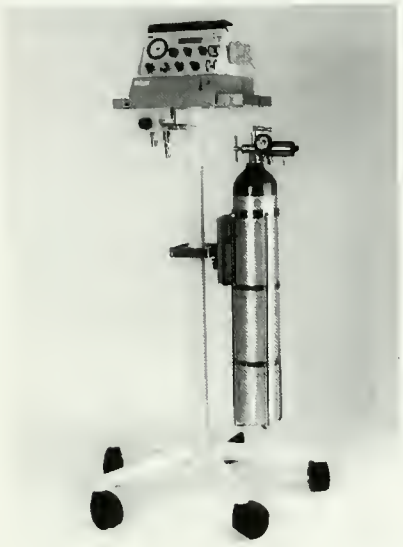
NOTEBOOK COMPUTER SYSTEM. The Explorer Notebook is a new lightweight compact electromyography (EMG)/evoked potential instrument by Bio-logic Systems Corporation. According to the company, the system includes software and hardware equivalent to a full-size desktop model. The display provides real-time EMG, 8 traces, measurements, and tables. The 100 MHz portable notebook computer offers a 2-channel (expandable to 8) base system, built-in speaker, automatic report generation, 7-button remote control unit, and a carrying case with storage for accessories. For information about the system, circle Reader Service Number 162.

NASAL MASK. Respironics Inc now includes the Monarch™ Mini Mask nasal interface for treating adult obstructive sleep apnea. The mask can be used with continuous positive airway pressure and bi-level positive airway pressure systems, according to Respironics. The mask features the Comfort Seal, developed to provide comfort while maintaining a seal. (If leaks do occur, they are away from the eyes and may be more tolerable to patients.) In addition, headgear helps hold the mask in place, and one-size nasal mask fits a wide range of patients. Circle Reader Service Number 163 for more information from Respironics.

BIOPSY NEEDLE. Popper & Sons Inc reports the availability of the O & S Biopsy Needle. The needle, according the company, can be used in patients with pleural effusion and yields larger pleural specimens. The O & S Needle has a self-opening biopsy flap that helps prevent injury to the lung during the biopsy procedure. The external diameter of the needle is 3 mm—smaller then other biopsy needles. For details, circle Reader Service Number 164.

STRESS/HOLTER SYSTEM. Oxford Instruments issues Medilog® StressLink, an exercise management system. According to a company press release, the StressLink features Oxford's Medilog Holter program and an electrocardiogram (ECG) management system. The 2-in-1 instrument provides either Holter or stress functions. Patient records and databases are fully compatible with Mi-

crosoft® computer systems and can be correlated for reports. For information about the system, circle Reader Service Number 165.



MULTIPURPOSE VENTILATOR. Dräger Inc provides the MicroVent compact, portable ventilator. The new design features assist/control, synchronized intermittent mechanical ventilation, pressure support, continuous positive airway pressure, apnea ventilation, and optional pressure control ventilation. According to the manufacturer, the ventilator also offers flow trigger with base flow, adjustable inspiratory time, a bi-directional flow sensor, and an internal rechargeable battery. In addition, the MicroVent is compact and lightweight and offers monitors and alarms. To contact Dräger for more information, circle Reader Service Number 166.

NASAL MASK. Respironics Inc discloses the GEL™ Mask for use in the treatment of adult obstructive sleep apnea. The nasal mask features a unique, soft gel-like material cushion that allows the mask to seal with less headgear tension, the company says. Designed to closely match the contours of the face, the cushion helps create a seal around the cheeks and nose. In addition, the GEL Mask works with most continuous positive airway pressure and bi-level positive airway pressure systems and is available in 7 sizes to fit a variety of patients. Information is available from Respironics; circle Reader Service Number 167.

DATA MANAGEMENT SYSTEM. Diametrics Medical Incorporated releases the IRMA® Data Management System (IDMS). The software program provides data management for point-of-care testing technologies. Although initially developed for the IRMA Blood Analysis System, the IDMS version 3.0 features a wider range of compatibility, works well with other programs, and is network compatible, according to the company. The system stores, organizes, and centralizes data for analysis in database functions and facilitates rapid transfer of blood tests and quality control results from the point of care to the larger hospital information system. Circle Reader Service Number 168 for more facts.

HAZARDOUS MATERIAL DISPOSAL. PCI Medical Inc releases the Glutaraldehyde User Station. The system is designed to reduce the risks associated with carrying trays of used glutaraldehyde and exposures to fumes, claims the company. The system uses a suction tube to pump the used chemical out of the bowl and out through the discharge tube to a sink or hopper. Technical data about the system is available; circle Reader Service Number 169.

COLD WEATHER MASK. The Alaskan BreathWarmer cold weather mask is released by Weber & Sons Inc. The mask is made to conserve body heat for people who participate in cold weather activities or working conditions or for those with cardiac or respiratory problems, the company says. Furthermore, the mask helps prevent the loss of body heat by warming and humidifying each inhaled breath by retrieving most of the heat and moisture from the preceding exhaled breath. Breath-activated valves help prevent fogged glasses and the formation of ice on the outside of the mask. A removable metallic heat exchange pack can be cleaned, and the mask is made of sturdy plastic with a soft, flexible rubber gasket for a more comfortable fit and seal around the nose and mouth. Adjustable elastic straps hold the mask firmly on the user's head. Circle Reader Service Number 170 for details from the company.

SPACER. The E-Z Spacer® is currently available from WE Pharmaceuticals Inc. The spacer is a portable drug delivery system designed for use with metered dose inhalers. WE literature reports that the spacer is a 700-mL drug delivery system that targets medication to the lungs and reduces upper airway deposition. The clear reservoir bag is easy to clean and allows the patient to see its aerosol content. The entire unit is collapsible for easy carrying. Circle Reader Service Number 171 for details about the spacer.

RESPIRATORY CARE

Manuscript Preparation Guide

General Information

RESPIRATORY CARE welcomes original manuscripts related to respiratory care and prepared according to these Instructions. Manuscripts are blinded and reviewed by professionals who are experts in their fields. Authors are responsible for all aspects of the manuscript and receive galleys to proofread before publication. Each accepted manuscript is copyedited so that its message is clear and it conforms to the Journal's style. Published papers are copyrighted by Daedalus Inc and may not be published elsewhere without permission.

Editorial consultation is available at any stage of planning or writing. On request, specific guidance is provided for all publication categories. These Instructions and related materials are available. Write to RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229-4593, call (972) 243-2272, or fax (972) 484-6010.

Publication Categories & Structure

Research Article: A report of an original investigation (a study). It includes a Title Page, Abstract, Introduction, Methods, Results, Discussion, Conclusions, Product Sources, Acknowledgments, References, Tables, Appendices, Figures, and Figure Captions.

Evaluation of Device/Method/Technique: A description and evaluation of an old or new device, method, technique, or modification. It has a Title Page, Abstract, Introduction, Description of Device/Method/Technique, Evaluation Methods, Evaluation Results, Discussion, Conclusions, Product Sources, Acknowledgments, References, Tables, Appendices, Figures, and Figure Captions.

Case Report: A report of a clinical case that is uncommon, or was managed in a new way, or is exceptionally instructive. All authors must be associated with the case. A case-managing physician must either be an author or furnish a letter approving the manuscript. Its components are Title Page, Abstract, Introduction, Case Summary, Discussion, References, Tables, Figures, and Figure Captions.

Review Article: A comprehensive, critical review of the literature and state-of-the-art summary of a pertinent topic that has been the subject of at least 40 published research articles. Title Page, Outline, Introduction, Review of the Literature, Summary, Acknowledgments, References, Tables, Appendices, and Figures and Captions may be included.

Overview: A critical review of a pertinent topic that has fewer than 40 published research articles.

Update: A report of subsequent developments in a topic that has been critically reviewed in this Journal or elsewhere.

Point-of-View Paper: A paper expressing personal but substantiated opinions on a pertinent topic. Title Page, Text, References, Tables, and Illustrations may be included.

Special Article: A pertinent paper not fitting one of the foregoing categories may be acceptable as a Special Article. Consult with the Editor before writing or submitting such a paper.

Editorial: A paper drawing attention to a pertinent concern; it may present an opposing opinion, clarify a position, or bring a problem into focus.

Letter: A signed communication about prior publications in this Journal or about other pertinent topics. Tables and illustrations may be included. Mark "For publication."

Blood Gas Corner: A brief, instructive case report involving blood-gas values—with Questions, Answers, and Discussion.

Drug Capsule: A mini-review paper about a drug or class of drugs that includes discussions of pharmacology, pharmacokinetics, and pharmacotherapy.

Graphics Corner: A brief case report incorporating waveforms for monitoring or diagnosis—with Questions, Answers, and Discussion.

Kittredge's Corner: A brief description of the operation of respiratory care equipment—with information from manufacturers and editorial comments and suggestions.

PFT Corner: Like Blood Gas Corner, but involving pulmonary function tests.

Cardiorespiratory Interactions. A case report demonstrating the interaction between the cardiovascular and respiratory systems. It should be a patient-care scenario; however, the case—the central theme—is the systems interaction. CRI is characterized by figures, equations, and a glossary. See the March 1996 issue of RESPIRATORY CARE for more detail.

Test Your Radiologic Skill: Like Blood Gas Corner, but involving pulmonary medicine radiography and including one or more radiographs, may involve imaging techniques other than conventional chest radiography.

Review of Book, Film, Tape, or Software: A balanced, critical review of a recent release.

Preparing the Manuscript

Print on one side of white bond paper, 8.5 in. x 11 in. (216 x 279 mm) with margins of at least 1 in. (25 mm) on all sides of the page. Use ***double-spacing*** throughout the ***entire*** manuscript. Use

a standard font (eg, Times, Helvetica, or Courier) at least 10 points in size, and do not use italics except for special emphasis. Number all pages in upper-right corners. Indent paragraphs 5 spaces. Do ***not justify***. Do ***not*** put authors' names or other identification anywhere except on the title page. Repeat title only (no authors) on the abstract page. Begin each of the following on a new page: Title Page, Abstract, Text, Product-Sources List, Acknowledgments, References, each Table, and each Appendix. Use standard English in the first person and active voice.

Center main section headings on the page and type them in capital and small letters (eg, Introduction, Methods, Results, Discussion). Begin subheadings at the left margin and type them in capital and small letters (eg, Patients, Equipment, Statistical Analysis).

References. Cite only published works as references. Manuscripts accepted but not yet published may be cited as references: designate the accepting journal, followed by (in press). Please provide 3 copies of the in-press article for reviewer inspection. Cite references in the text with superscript numerals. Assign numbers in the order that references are first cited. On the reference page, list the cited works in numerical order. Follow the Journal's style for references. Abbreviate journal names as in *Index Medicus*. List all authors.

Article in a journal carrying pagination throughout volume:

1. Rau JL, Harwood RJ. Comparison of nebulizer delivery methods through a neonatal endotracheal tube: a bench study. Respir Care 1992;37(11):1233-1240.

Article in a publication that numbers each issue beginning with Page 1:

2. Bunch D. Establishing a national database for home care. AARC Times 1991;15(Mar):61,62,64.

Corporate author journal article:

3. American Association for Respiratory Care. Criteria for establishing units for chronic ventilator-dependent patients in hospitals. Respir Care 1988;33(11):1044-1046.

Article in journal supplement: (Journals differ in their methods of numbering and identifying supplements. Supply sufficient information to promote retrieval.)

4. Reynolds HY. Idiopathic interstitial pulmonary fibrosis. Chest 1986;89(3, Suppl):139S-143S.

Abstract in journal: (Abstracts citations are to be avoided. Those more than 3 years old should not be cited.)

5. Stevens DP. Scavenging ribavirin from an oxygen hood to reduce environmental exposure (abstract). Respir Care 1990;35(11): 1087-1088.

Editorial in journal:

6. Enright P. Can we relax during spirometry? (editorial). Am Rev Respir Dis 1993;148(2):274.

Editorial with no author given:

7. Negative-pressure ventilation for chronic obstructive pulmonary disease (editorial). Lancet 1992;340(8833):1440-1441.

Letter in journal:

8. Aelony Y. Ethnic norms for pulmonary function tests (letter). Chest 1991;99(4):1051.

Paper accepted but not yet published:

9. Hess D. New therapies for asthma. Respir Care (year, in press).

Personal author book: (For any book, specific pages should be cited whenever possible.)

10. DeRemee RA. Clinical profiles of diffuse interstitial pulmonary disease. New York: Futura, 1990:76-85.

Corporate author book:

11. American Medical Association Department of Drugs. AMA drug evaluations, 3rd ed. Littleton CO: Publishing Sciences Group, 1977.

Chapter in book with editor(s):

12. Pierce AK. Acute respiratory failure. In: Guenter CA, Welch MH, editors. Pulmonary medicine. Philadelphia: JB Lippincott, 1977.

Tables. Use consecutively numbered tables to display information. Start each table on a separate page. Number and title the table and give each column a brief heading. Place explanations in footnotes, including all nonstandard abbreviations and symbols. Key the footnotes with conventional designations (asterisk, dagger, double dagger, etc) in consistent order, placing them superscript in the table body. Do not use horizontal or vertical rules or borders. Do not submit tables as photographs, reduced in size, or on oversize paper. Use the same typeface as in the text.

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Bach, John R 403
Hess, Dean 424
Hill, Nicholas S 394, 432
Kacmarek, Robert M 380
Pierson, David J 370
Rubenfeld, Gordon D 443
Teague, W Gerald 414
Turner, Robert E 389
Wunderink, Richard G 394

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140	141	142	143	144	145	146	147	148	149	150	151	152	153	154
155	156	157	158	159	160	161	162	163	164	165	166	167	168	169
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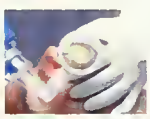

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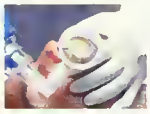
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